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# Dosimetric Comparison of Volumetric Modulated Arc Therapy Treatment Plans using Pareto and Constrained Modes of Optimization with Monaco Treatment Planning System for Left Breast Cancer with Breast Conserving Surgery

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ABSTRACT

***Introduction:*** Volumetric Modulated Arc Therapy (VMAT) is an advanced method of radiation therapy with increased flexibility in intensity modulation. The study aims to compare the dosimetric outcomes of VMAT treatment plans generated using Pareto and Constrained modes of optimization for left breast cancer with breast-conserving surgery (BCS).

***Material and Methods:*** We carried out a retrospective study of twenty female patients who underwent BCS for left breast cancer. VMAT treatment plans were generated using two optimization modes, Pareto and Constrained, on the Monaco (version 5.11.03) treatment planning system (TPS), with a single arc of 6MV x-ray photon beam from Elekta Versa HD linear accelerator (linac). The prescribed dose was 42.56 Gray (Gy) in 16 fractions to the PTV. Dosimetric parameters, such as the target volume coverage, organs at risk (OARs) doses, homogeneity index (HI), as well as conformity index (CI), were studied and compared between the two modes of optimization using the Wilcoxon signed-rank test (Jamovi 2.3.26).

***Results:*** The study showed that the Pareto mode of optimization within VMAT gave superior outcomes, with increased coverage of the target and comparable OAR doses. However, there is a slight increase in the volume receiving 107% of the prescribed dose ($V_{107}$), maximum dose ($D_{max}$) within the target volume, and monitor units (MU); the HI and CI show excellent performance.

***Conclusion:*** This study suggests that Pareto mode optimization in VMAT is a preferable and superior approach for left breast cancer patients undergoing BCS.

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## Introduction

Carcinoma of the breast is a configuration of cancer that originates on the tissues of either of the two breasts or both breasts [1]. It is the leading form of cancer in women, but even men can be affected. Globally, it ranks as the second most common cause of cancer-related fatalities among women [2], [3]. It comes up mainly in the cells that line the lobules in the glandular tissue of the breast that produces the milk, or the small channels called ducts that protrude from the lobules and transport milk to the nipple [4]. The diagnostic tests carried out for the detection of the tumor include mammography, ultrasound of the breast, magnetic resonance imaging of the breast, and biopsy [5]. The patient's breast cancer type and stage, along with their overall health status and treatment preferences, all influence the choice of a particular course of action [6]. The patient either undergoes BCS or modified radical mastectomy (MRM) as the initial step in medical intervention [7]. There are several adjuvant therapies for breast cancer following surgery, such as radiation therapy that includes brachytherapy and external beam radiation therapy (EBRT), chemotherapy, hormone therapy, immunotherapy, and so on [8, 9].

The EBRT technique allows for precise radiation targeting of the tumor while minimizing damage to healthy tissues [10]. Three-dimensional conformal radiation therapy (3DCRT), IMRT, and VMAT are the techniques practiced in radiotherapy to treat breast cancer [11], [12]. According to research, IMRT and VMAT are the most advanced radiation therapy

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techniques used for treating breast cancer patients [13], [14]. VMAT comes up with a more rapid treatment than static field IMRT [15], [16]. Radiation therapy treatment planning is crucial in reducing radiation exposure to the contralateral breast, the ipsilateral and contralateral lungs, and the heart [17]. For patients with left breast cancer, it is recommended to consider Voluntary Deep Inspiration Breath Hold (V-DIBH) as it can effectively reduce the doses to the heart and ipsilateral lung when compared to Free Breathing (FB). However, not all patients are able to undergo V-DIBH due to varying levels of support [18]. VMAT helps determine an efficient plan for delivering an even dose to the target volume while minimizing radiation exposure to OARs [19]. This is accomplished through a linear accelerator (linac) when the radiation beam continuously rotates around the patient, enabling precise adjustments in beam intensity, gantry movement, and multi-leaf collimator (MLC) positions. Radiation is thus distributed uniformly, reducing the possibility of adverse effects [20].

VMAT offers two optimization modes, Pareto and Constrained, to help generate treatment plans [21]. In the Pareto mode, the system prioritizes coverage of the target before trying to satisfy the constraints of the OARs, while in the Constrained mode, the system achieves OAR constraints prior to attaining the target coverage [22]. There are limited studies that directly compare the performance of the Pareto and constrained modes of optimization within VMAT. In contrast to the studies that focus on organs like the heart and the ipsilateral lung as potential OARs to treat left breast cancer, we have expanded our analysis to include other vital structures, such as the right lung, the right breast, as well as the spinal cord. These OARs were chosen because of their proximity to the volume of the target. The main goal of this study is to compare the dosimetric results of the treatment plans that were optimized using both modes.

## Materials and Methods

Twenty female patients who had left-sided breast cancer and underwent BCS were selected retrospectively for this study. During the image acquisition, the patients were positioned head-first supine on a flat couch with their arms raised. They were immobilized with a thermoplastic mask called ORFIT to ensure a stable position throughout the procedure. The CT images of the patient were acquired using a Philips Brilliance Big Bore 16-slice CT scanner with a slice thickness of 5mm. The Monaco (version 5.11.03) TPS was used to analyze the reconstructed images and delineate the target volumes and OARs according to RTOG guidelines [23]. The tumor's size and location, suspected to be present, are known as the Gross Tumor Volume (GTV). The Clinical Target Volume (CTV) is determined, including the GTV and any visible extensions of the tumor and any microscopic spread to nearby internal mammary nodes. To ensure that the radiation dose is received only by the tumor and not by healthy surrounding tissue, a margin of 3 to 5 mm was added around the CTV to create the Planning Target Volume (PTV). Also, the OARs were delineated, and the constraints were set such as, for each lung, with the volume getting 20 Gy not to exceed 20% and the volume receiving 25 Gy for the heart not to exceed 10%, the mean dosage to the contralateral breast was kept at less than 5 Gy, and the maximum dose that the spinal cord could receive was limited to less than 46 Gy. These limits were put in place to minimize radiation exposure to vital structures and mitigate any possible adverse effects [24].

***Treatment Planning System***

Monaco TPS (version 5.11.03), developed by Elekta, was used to generate the treatment plans of the selected patients for VMAT by using two different optimization modes, constrained and Pareto [25]. VMAT employs the Monte-Carlo algorithm for dose calculations [26], [27]. Monaco employs a two-step process for achieving optimal dose distribution: fluence beam optimization, followed by beam segmentation [28]. The plans for treatment were developed using a single arc of 6MV x-ray photon beam with 80 pairs of multileaf collimators of Elekta Versa High Definition (HD) linac, for the prescribed dose of 42.56 Gray (Gy) in 16 fractions to the PTV. The gantry start angle ranged between 300º-310º, with an arc span ranging between 180º-200º, setting the arc in a clockwise direction, and the grid size to 0.3cm for dose calculation. To optimize the target dose, biological cost functions were defined using the target equivalent uniform dose (EUD), quadratic overdose, and target penalty terms. The prescribed target dose was expressed in terms of EUD in the IMRT constraints tab. The specific cost function and maximum dosage were applied to the structure of the patient's body, together with the "optimize over all voxels in volume" option, in order to reduce the high dose volume in the patient's body and the target volume. The lowest acceptable criterion for both treatment schemes needed at least 95% coverage of the PTV by 95% of the prescribed dose.

***Plan Evaluation***

The optimal treatment plans generated using both optimization methods for each patient were assessed by comparing various dosimetric parameters for the target and OARs. The Dosimetric parameters obtained and evaluated were volume receiving 95% of the prescribed dose ($V_{95}$), volume receiving 107% of the prescribed dose ($V_{107}$), $D_{max}$ within the target volume, $D_{mean}$ for contralateral breast, volume receiving 20Gy ($V_{20}$) for the ipsilateral lung as well as the contralateral lung, volume receiving 25Gy ($V_{25}$) for the heart, $D_{max}$ to the spinal cord, HI, CI and MU delivered.

***Homogeneity Index***

The HI is a parameter in radiation therapy treatment planning to assess the uniformity of dose distribution within the target volume. An HI value of 1 is considered ideal as an indication of absolute homogeneity. However, HI values above 1 signify deteriorating homogeneity in the plan.

The formula to calculate the HI is given by:

$$HI=(D_{5\%}-D_{95\%})/D_{pres} \quad (1)$$

Here, $D_{5\%}$ is the minimum dose in 5% of the target volume, $D_{95\%}$ is the minimum dose in 95% of the target volume, and $D_{pres}$ is the dose prescribed [29].

***Conformity Index***

The CI is a tool used in radiation therapy treatment planning to assess the coverage of the target volume. The ideal value for CI is 1, which indicates that the prescribed dose is delivered only to the target volume. If the CI is greater than 1, it means that the volume of tissue receiving the prescribed dose exceeds the volume of the target.

The formula to calculate the CI is given by:

$$CI = (V_{95\%} / V_{PTV}) \times (V_{95\%} / TIV_{95\%}) \quad (2)$$

Here, $V_{PTV}$ refers to the volume of PTV, and $TIV_{95\%}$ refers to the total irradiated volume of the body covered with 95% of the recommended dose [29].

## Results

The dose distribution to the target and OARs, along with their dose volume histograms (DVH) for both optimization modes, is shown in Figures 1 and 2 respectively.

To compare the outcomes of the two optimization modes, a non-parametric statistical test called Wilcoxon signed-rank analysis was performed (Jamovi 2.3.26). Table 1 presents the mean and standard deviation values for the different dosimetric quantities, along with their significant (p) values, providing a summary of their respective statistical measures. The results of the test indicate whether there is a significant difference between the outcomes of the two optimization methods. The statistical findings of the analysis have been examined and evaluated.

Graphs were developed to visually represent several planning parameters, making the dosimetric study easier to comprehend and interpret. As shown in Figure 3, in the Pareto mode of optimization, the $V_{95}$ of the PTV was measured to be 92.200±4.780, while in the Constrained mode, it was 90.800±4.220, however, these values had no statistically significant difference, with a p-value of 0.475, also, the relative volume of the PTV encompassed by 107% of the prescribed dose differed significantly between the Pareto and Constrained modes. In the Pareto mode, it was 1.757±1.328, whereas, in the Constrained mode, it was 0.450%±0.731%, with a p-value of less than 0.001.

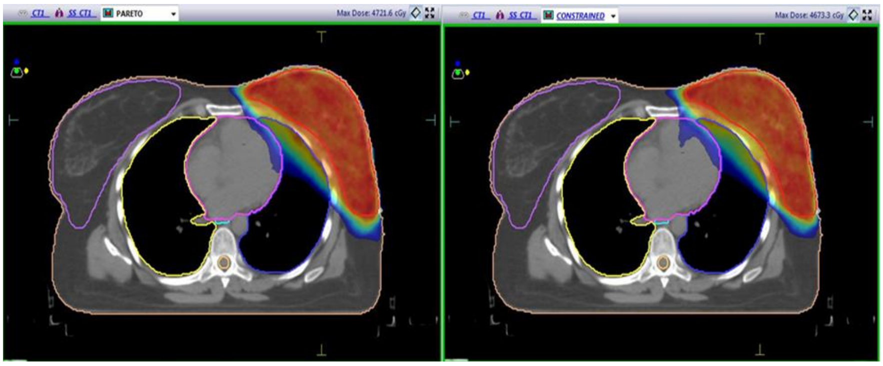


Figure 1. Dose distribution to the target volume and the OARs in the Pareto and Constrained modes of optimization, respectively

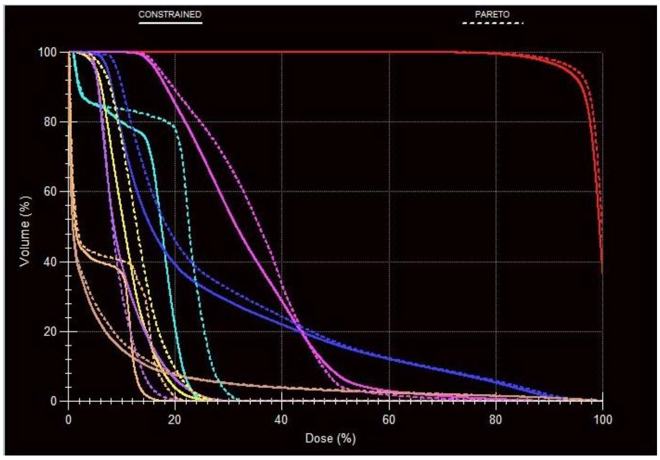


Figure 2. DVH of Pareto and Constrained modes of optimization

The $D_{max}$ received by the PTV varied in the Pareto mode, ranging from 4622.500 cGy to 5017.600 cGy, with an average of 4833.000±106.000 and in the Constrained mode, it ranged from 4468.100 cGy to 5019.300 cGy, with an average of 4727.000±121.000 is represented in figure 4. These differences were statistically significant, with a p-value of less than 0.001. The mean dose ($D_{mean}$) to the contralateral breast in the Pareto and Constrained modes of optimization were 417.000±137.000 and 425.000±121.000, respectively. Still, again, there was no statistically significant difference, with a p-value of 0.430, as represented in Figure 5. Figure 6 shows the $V_{20}$ values for the left lung that were found to be 16.600±5.330 in the Pareto mode and 16.600±2.860 in the Constrained mode, with no statistically significant difference (p-value = 0.674) and the right lung with the values to be 0.190±0.356 in the Pareto mode and 0.272±0.485 in the Constrained mode, with a p-value of 0.193.

Table 1. Ranking of plan parameters based on p-value

| Parameters | Pareto Mean ± SD | Constrained Mean ± SD | p-value |
|---|---|---|---|
| $V_{107}$ for PTV (%) | 1.757±1.328 | 0.450±0.731 | < 0.001 |
| Maximum Dose within PTV (cGy) | 4833.000±106.000 | 4727.000±121.000 | < 0.001 |
| Monitor Units (MU) | 1338.000±281.000 | 1160.000±225.000 | < 0.001 |
| Conformity Index | 0.838±0.058 | 0.813±0.071 | 0.053 |
| Homogeneity Index | 0.131±0.059 | 0.118±0.048 | 0.165 |
| $V_{20}$ for Contralateral Lung (%) | 0.190±0.356 | 0.272±0.485 | 0.193 |
| Mean Dose within Contralateral Breast (cGy) | 417.000±137.000 | 425.000±214.000 | 0.430 |
| $V_{95}$ for PTV (%) | 92.200±4.780 | 90.800±4.220 | 0.475 |
| $V_{20}$ for Ipsilateral Lung (%) | 16.600±5.330 | 16.600±2.860 | 0.674 |
| $V_{25}$ for Heart (%) | 2.670±2.360 | 2.610±2.000 | 0.756 |
| Maximum Dose within Spinal Cord (cGy) | 1551.000±584.000 | 1559.000±648.000 | 0.898 |

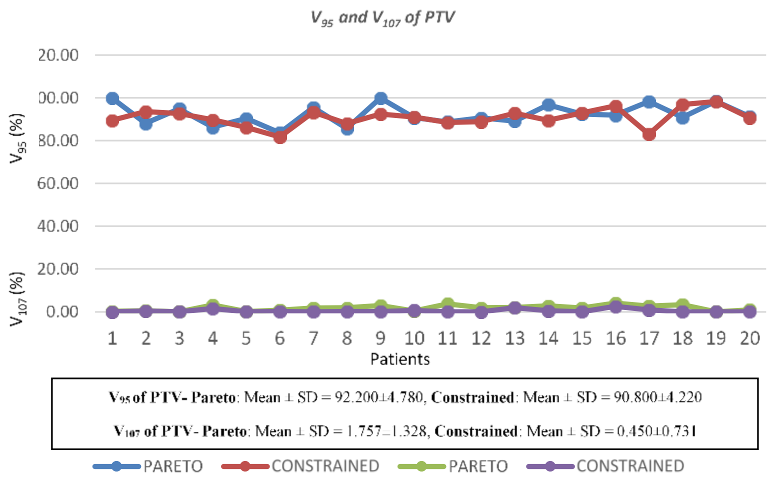


Figure 3. $V_{95}$ of PTV (p-value = 0.475) and $V_{107}$ of PTV (p-value = 0.001)

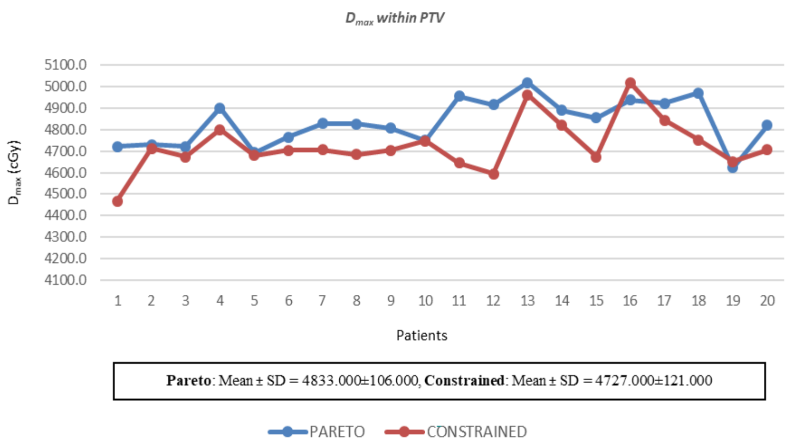


Figure 4. Maximum Dose within PTV (p-value < 0.001)

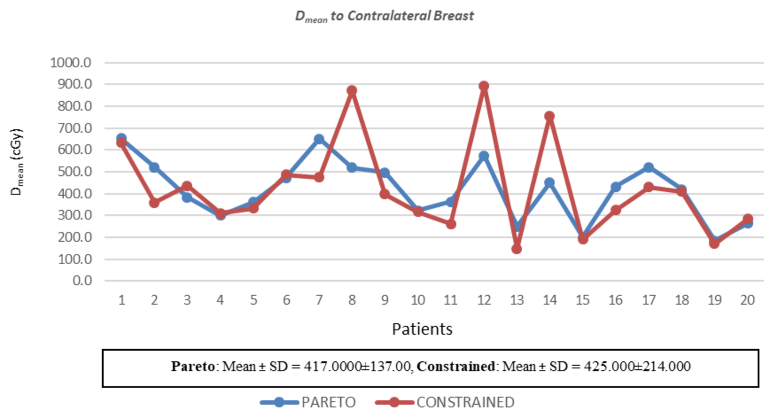


Figure 5. Mean Dose within Contralateral Breast (p-value = 0.430)

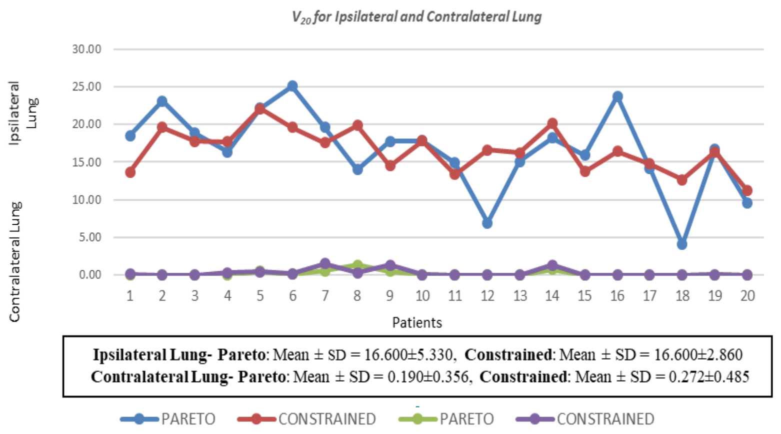


Figure 6. $V_{20}$ for Ipsilateral Lung (p-value = 0.674) and $V_{20}$ for Contralateral Lung (p-value = 0.193)

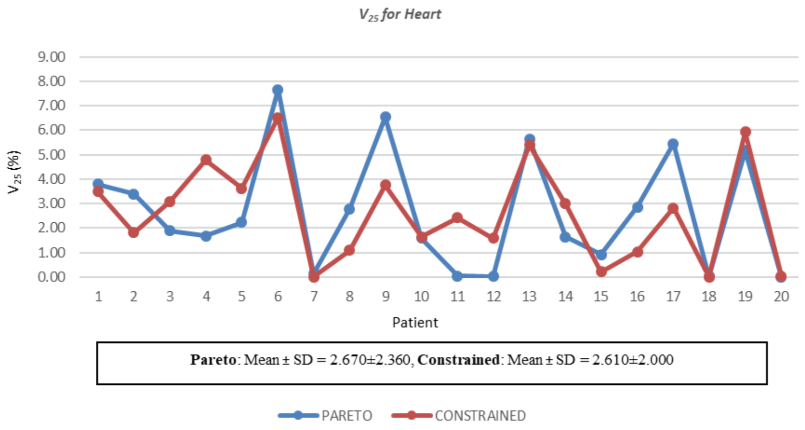


Figure 7. $V_{25}$ for Heart (p-value = 0.756)

Figure 7 shows that the $V_{25}$ of the heart values were 2.670±2.360 in the Pareto mode and 2.610±2.000 in the Constrained mode, but this difference was not statistically significant, with a p-value of 0.756.

The $D_{max}$ received by the spinal cord was 1551.000±584.000 in the Pareto mode and 1559.000±648.000 in the Constrained mode as represented in Figure 8, which is not statistically significant (p-value = 0.898). Figure 9 shows that the MU delivered in the Pareto and constrained modes were 1338.000±281.000 and 1160.000±225.000, respectively, and it is statistically significant with a p-value of less than 0.001. Figures 10 and 11 say that the HI and CI for the Pareto mode were obtained as 0.131±0.059 and 0.838±0.058, respectively, while for the constrained mode, they were 0.118±0.048 and 0.813±0.071, respectively. The p-value for the HI was 0.165, and for the CI, it was 0.053.

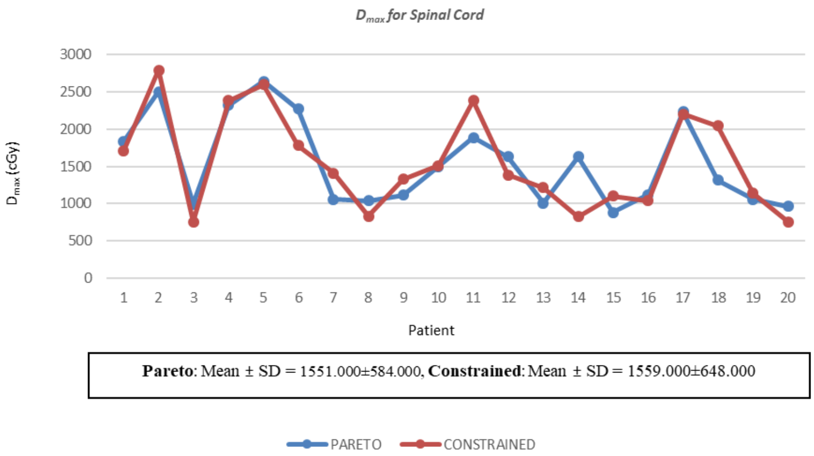


Figure 8. Maximum Dose within Spinal Cord (p-value = 0.898)

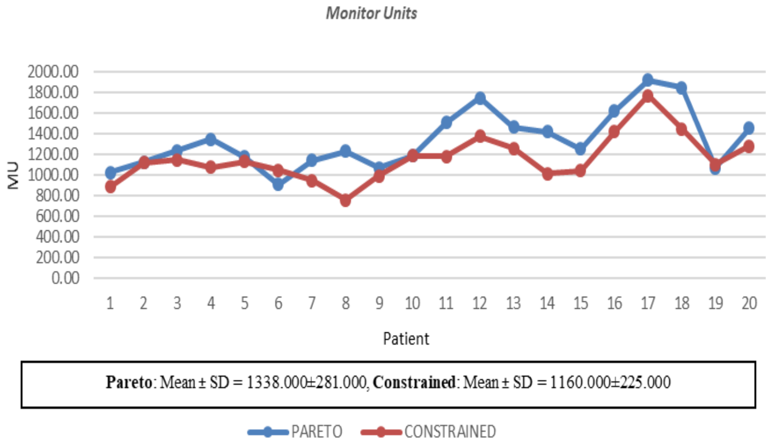


Figure 9. Monitor Units (p-value < 0.001)

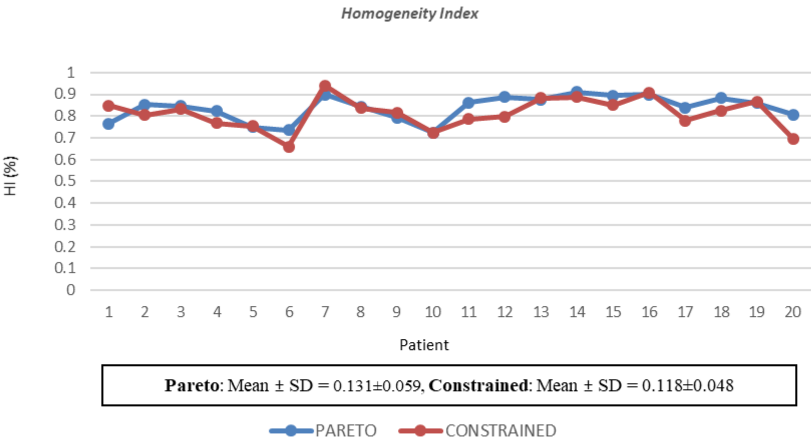


Figure10. Homogeneity index (p-value < 0.165)

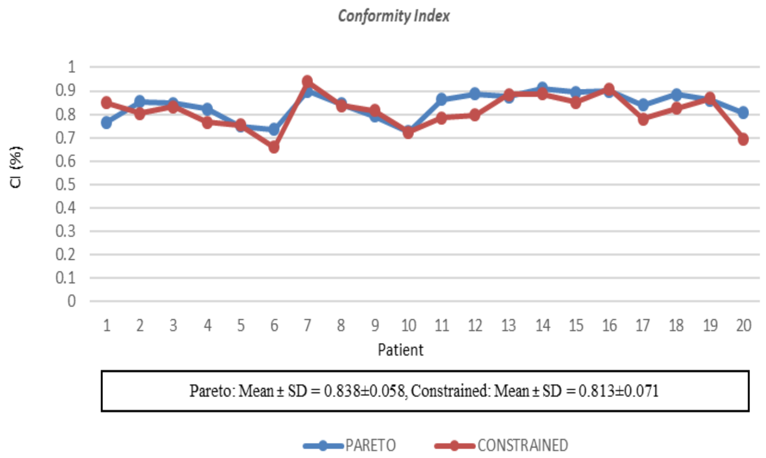


Figure 11. Conformity index (p-value < 0.053)

## Discussion

The results of the current study support the idea that using the Pareto mode for optimizing VMAT treatment plans might be a good option for treating breast cancer that is left-sided with BCS, as it achieves very good target coverage with comparable doses to OARs. However, it is to be observed that the $V_{107}$ in the PTV is slightly higher in the Pareto mode. The radiation doses are less to the ipsilateral and contralateral lungs, contralateral breast, and also to the spinal cord in Pareto mode. Incredibly, the dose to the heart is identical in both optimization modes. Furthermore, the Pareto mode has a slightly higher maximum dose to the PTV, $V_{107}$ for the PTV, and higher MU. Also, the Pareto mode demonstrates superior HI and CI compared to the Constrained mode, indicating better dose distribution and coverage.

These findings suggest that when plans are generated for VMAT using the Pareto optimization mode, the target receives excellent dose coverage with minimal OAR dosages. This further reduces the risk of acute or long-term toxicities, resulting in a better treatment option for the patients

These findings support the study conducted by Srivastava AK et al. that compared Pareto and Constrained modes of optimization for VMAT treatment plans generated for post-operated left breast cancer patients, with two arcs for 6MV x-ray photon beam from Elekta Infinity linac. Dosimetric quantities such as $V_{95}$, $V_{107}$, $D_{max}$ to the target volume, $D_{mean}$ for the heart, $V_{30}$, $V_{20}$, and $V_5$ for the left lung, and delivered MU were analyzed. Incredibly, the dose for the heart is similar in both optimization modes. Additionally, the Pareto mode has a slightly higher Dmax in the PTV, $V_{107}$ in the PTV, as well as the MU. Also, the Pareto mode witnessed superior HI and CI when compared to the constrained mode, which indicates greater coverage and distribution of doses [30].

Singh P et al. compared the dosimetric results of doses to the OARs in the treatment plans of conventional radiation therapy, IMRT, and VMAT for post-operated breast cancer patients. They found that VMAT plans, which were generated using the constrained mode of optimization, contributed in lesser doses to OARs as compared to the other two. They found that the doses received by $V_{20}$ of the ipsilateral lung, $V_{25}$ of the heart, $D_{mean}$ to the contralateral breast, and $D_{max}$ to the spinal cord were 29.6±3%, 5.4±4.9%, 4.1±0.9%, and 28.4±6.5% respectively [31]. Whereas our study found the Pareto mode of optimization to have given fewer dosages such as 16.6±5.33, 2.67±2.36, 417±137cGy, and 1551±584cGy to $V_{20}$ of the ipsilateral lung, $V_{25}$ of the heart, $D_{mean}$ to the contralateral breast, and $D_{max}$ to the spinal cord, respectively.

Pyshniak V et al. compared the VMAT treatment plans with biological and physical cost functions for prostate cancer using the Pareto mode of optimization, where they found that the Pareto mode provided good target coverage with reduced doses to the OARs. Also, the median dose to the bladder was reduced with increased conformity to the target is appreciable because of the usage of biological cost functions [32]. This study aligns with the study of Pyshniak V et al. in the means of $V_{95}$ of the PTV, comparable OAR doses, especially the lungs and heart, and better conformity of the target volume.

The sample size of twenty patients could be a limitation in this study. Conducting further research with a larger sample size could lead to enhancing the reliability of the findings.

## Conclusion

The findings of our study have shown that the Pareto mode optimization in VMAT treatment plans for radiation therapy is superior to the constrained mode. The Pareto mode results in better coverage of the target volume and minimal OAR dosages, which makes it the most effective option. Even though there is a slight increase in the hotspot, $D_{max}$ within the PTV and MU, the HI and CI have exceptional outcomes. These impressive findings conclude that the Pareto mode of optimizing VMAT treatment plans could be the most beneficial approach for patients undergoing BCS for left breast cancer.

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