3DCRTversus RapidArc treatment for breast cancer:dosimetric study

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Abstract: The Aim of this study is to compare (3D-CRT) to RapidArc planning systems using (LNAC of 6 MV, 15 MV and 18 MV) in terms of dosimetric outcomes of iso-dose distribution, dose volume histogram (DVH), PTV and at risk organs in 6 patients with breast cancer. The mean value of the PTV was (51.38 ± 2.172) in RapidArc compared to(52.21 ± 1.963) in 3D-CRT , which means that RapidArc plan achieved lower mean and maximum doses to the PTV.. RapidArc plan showed a more homogeneous dose distribution in PTV, achieving an HI of 1.262 ± 0.037 compared with 1.271 ± 0.024 in the 3D-CRT plan however, RapidArc and 3D-CRT achieved similar CI values and improvement in target coverage index (TCI) in which (TCI) in RapidArc was (0.006 ± 0.003) and (0.008 ± 0.006) in 3D-CRT, (P = 0.202). Volumetric modulated arc therapy (VMAT) is better than 3D-CRT in term of PTV, conformity and homogeneity for breast cancer.

Keywords: Planning Tumor Volume; Organs at Risk; Conformity Index; Heterogeneity Index; Breast cance

I. Introduction:

The optimal care of patients with malignant tumors is a multidisciplinary effort that combines classic modalities, surgery, radiation therapy, and chemotherapy. The role of the radiation oncologist is to assess all conditions relative to the patient and tumor, to systematically review the need for diagnostic and staging procedures, and, in consultation with other oncologists, determine the best therapeutic strategy. Radiation oncology includes the clinical and scientific discipline devoted to management of patients with cancer (and other diseases) with ionizing radiation (alone or combined with other modalities), investigation of the biologic and physical basis of radiation therapy, and training of professionals in the field. The aim of radiation therapy is to deliver a precisely measured dose of irradiation to a defined tumor volume with minimal damage to surrounding healthy tissue. This results in eradication of the tumor, increased quality of life, and prolongation of survival at a competitive cost, and allows for effective palliation or prevention of symptoms of cancer, including pain, restoring luminal patency, skeletal integrity, and organ function, with minimal morbidity[1, 2].The goal of therapy should be defined at the onset of therapeutic intervention: • Curative: There is a probability of long-term survival after adequate therapy. Some side effects of therapy, although undesirable, may be acceptable. • Palliative: There is no hope of survival for extended periods. Symptoms producing discomfort or an impending condition that may impair comfort or self-sufficiency require treatment. No major iatrogenic conditions should be observed. Relatively high doses of irradiation (sometimes 75% to 80% of the curative dose) are required to control the tumor for the survival period of the patient[3]. The basis for Prescription of Irradiation includes Evaluation of the extent of the tumor (staging), including diagnostic studies, knowledge of pathologic characteristics of the disease, definition of the goal of therapy (cure or palliation), selection of appropriate treatment modalities (irradiation alone or combined with surgery, chemotherapy, or both), determination of the optimal dose of irradiation and volume to be treated, according to anatomic location, histologic type, stage, potential regional nodal involvement (and other tumor characteristics), and normal structures in the region. It also includes evaluation of the patient's general condition, plus periodic assessment of tolerance to treatment, tumor response, and status of normal tissues treated and Ultimate responsibility for treatment decisions, technical execution of therapy, and consequences of therapy always rests with the radiation oncologist[1, 4].Different irradiation doses are required for various probabilities of tumor control, depending on the tumor type and the initial number of clonogenic cells present. Various radiation doses can be delivered to specific portions of

the tumor periphery versus central portion) or to the tumor bed in cases in which the entire gross tumor has been surgically removed. The International Commission on Radiation Units and Measurements Reports Nos. 50 and 62 define the following treatment planning volumes[5, 6]. Gross tumor volume (GTV): all known gross disease, including abnormally enlarged regional lymph nodes. To determine GTV, appropriate computed tomography (CT) window and level settings that give the maximum dimension of what is considered potential gross disease must be used. Clinical target volume (CTV): Encompasses GTV plus regions considered to harbor potential microscopic disease. Planning target volume (PTV): provides margin around CTV to allow for internal target motion, other anatomic motion during treatment (e.g., respiration), and variations in treatment setup. PTV does not account for treatment machine beam characteristics[7]. Treatment portals must adequately cover all treatment volumes plus a margin to account for beam physical characteristics, such as penumbra. Simulation is used to accurately identify target volumes and sensitive structures and to document configuration of portals and the target volume to be irradiated. Treatment aids (e.g., shielding blocks, molds, masks, immobilization devices, compensators) are extremely important in treatment planning and delivery of optimal dose distribution. Repositioning and immobilization devices are critical because the only effective irradiation is that which strikes the clonogenic tumor cells[8]. Simpler treatment techniques that yield an acceptable dose distribution are preferred over more costly and complex ones, which may have a greater margin of error in day-to-day treatments. Accuracy is periodically assessed with portal (localization) films or on-line (electronic portal) imaging verification devices. Portal localization errors may be systematic or may occur at random [7].

CT simulation allows for a more accurate definition of target volume and anatomy of critical normal structures, three-dimensional (3-D) treatment planning to optimize dose distribution, and radiographic verification of the treated volume[9]. Advances in computer technology have augmented accurate and timely computation, display of 3-D radiation dose distributions, and dose-volume histograms that yield relevant information for the evaluation of tumor extent, definition of target volume, delineation of normal tissues, virtual simulation of therapy, generation of digitally reconstructed radiographs, design of treatment portals and aids, calculation of 3-D dose distributions and dose optimization, and critical evaluation of the treatment plan[10]. Dose-volume histograms are useful in assessing several treatment plan dose distributions and providing a complete summary of the entire 3-D dose matrix, and showing the amount of target volume or critical structure receiving more than the specified dose. They do not

provide spatial dose information and cannot replace other methods of dose display[11]. 3-D treatment planning systems play an important role in treatment verification. Digitally reconstructed radiographs based on sequential CT slice data generate a simulation film that can be used in portal localization and for comparison with the treatment portal film for verifying treatment geometry[12]. Increased sophistication in treatment planning requires parallel precision in patient repositioning and immobilization, as well as in portal verification techniques. Several real-time, on-line verification systems allow monitoring of the position of the area to be treated during radiation exposure. Computer-aided integration of data generated by 3-D radiation treatment planning with parameters used on the treatment machine, including gantry and couch position, may decrease localization errors and enhance the precision and efficiency of irradiation[13].

Intensity-modulated radiation therapy (IMRT), a new approach to 3-D treatment planning and conformal therapy, optimizes delivery of irradiation to irregularly shaped volumes through complex forward or inverse treatment planning and dynamic delivery of irradiation that results in modulated fluency of multiple photon beam profiles. Inverse planning starts with an ideal dose distribution and identifies, through trial and error or multiple iterations (simulated annealing), the beam characteristics (fluence profiles). It then produces the best approximation of the ideal dose defined in a 3-D array of dose voxels organized in a stack of two-dimensional arrays[12]. Other approaches to achieve IMRT include the step-and-shoot method, with a linear accelerator and multileaf collimation (MLC), which uses a variety of portals at various angles. The MLC determines photon-modulated fluency and portal shape by the dynamic computer-controlled IMRT being delivered when the configuration of the portals with the MLC changes at the same time that the gantry or accelerator changes positions around the patient... In helical tomotherapy, a photon fan beam continually rotates around the patient as the couch transports the patient longitudinally through a ring gantry. The robotic arm IMRT system (Cyberknife) consists of a miniaturized MV photon linear accelerator mounted on a highly mobile arm and a set of ceiling-mounted x-ray cameras to provide near real time information on the patient's position and target exposure during treatment[14]. The majority of IMRT systems use 6 MV x-rays, but energies of 8 to 10 MV may be more desirable in some anatomic sites to decrease skin and superficial subcutaneous tissue dose[15].A comprehensive quality assurance (QA) program is critical to ensure the best treatment for each patient and to establish and document all operating policies and procedures. QA procedures in radiation therapy vary, depending on whether standard treatment or a clinical trial is carried out, and if such treatments and trials occur at single or multiple institutions. In multi-institutional studies, it is important to

provide all participants with clear instructions and standardized parameters in dosimetry procedures, treatment techniques, and treatment[16].The concept of IMRT was not applied until the 1990s. The software and hardware were not available before that time[17]. IMRT is a more advanced mode of conformal radiotherapy and an extension of 3-dimensional conformal radiation therapy (3D-CRT) that includes the use a larger number of x-ray beam compared to 3D-CRT. Therefore, large volumes of healthy tissue are exposed to low levels of radiation [18, 19]. IMRT allows for appropriate conforming of the high and low doses to the target and healthy tissue, by creating non-uniform radiation beam intensities across the irradiation field. This creation can be performed in two ways: step and shoot (static technique) or sliding window (dynamic technique) [14, 19, 20]. Intensity modulated arc therapy (IMAT) is the next step in IMRT radiation delivery, whereby the gantry rotates around the patient and the radiation dose is delivered continuously in an arc[14]. It is possible to summarize the advantages of IMRT in good sparing to critical structures and fairly quick planning. However, the disadvantages include complex QA and longer treatment time.

Volumetric modulated arc therapy (VMAT) is a novel from of IMRT that allows the radiation to be delivered to the patient in a single 360◦ of gantry rotation that is accurately and efficiently with varying velocities and positions of the MLC, dose rate and gantry speed. This leads VMAT being an intensity-modulated dose distribution[21]. RapidArc (Varain medical system) is a form of VMAT[22]. RapidArc (RA) is intended to protect healthy tissue more than other techniques and to improve target coverage distribution and treatment time, and attain accurate dosimetric delivery to have the ideal dose distribution. VMAT has many different advantages over conventional modality 3D-CRT[20]. The fundamental feature is treatment time. VMAT treatment time was 1.3 minutes, IMRT treatment time was 8 minutes and 3D-CRT was 3 minutes[23].Other studies have demonstrated a similar decline in treatment time between VMAT and 3D-CRT. Depending on decreased treatment time in the machine, patient comfort, compliance and throughput increased. The main disadvantage of VMAT is the increased optimization time compared to 3D-CRT. Shannon M. MacDonald et al[24], compared 3D-CRT with IMRT for 20 patients treated for high – grade glioma. The prescribed dose was 59.4 Gy. The authors showed that IMRT was superior in target coverage compared with 3D-CRT plans, and effectively reduced radiation dose to the brain, brain stem and optic chiasm. David Palam et al.[21] compared three techniques: VMAT, IMRT and 3D-CRT for 10 patients with prostate cancer. The comparison showed lower doses to normal critical structure and achieved highly conformal treatment plans in VMAT and IMRT over 3D-CRT plans. Luca Cozzi et al.[25] used a treatment planning system to compare

Volumetric Arc Modulation with RapidArc and IMRT for cervix uteri of 8 patients. Both RA and IMRT showed equivalent target coverage. RA improved CI, HI and OARs sparing. Wilko F.A.R Verbakel et al.[26] compared VMAT with conventional IMRT in 12 patients for head and neck cancer. The dosimetric benefit of applying volumetric modulated arc therapy (VMAT) on the post-mastectomy left-sided breast cancer patients, with the involvement of internal mammary nodes (IMN) compared with intensity-modulated radiotherapy (IMRT) plans on Pinnacle treatment planning system showed showed similar PTV dose homogeneity, but, VMAT provided a better dose coverage for IMN than IMRT [27] .

2. Material and Methods

A. Equipment Used

A.1. Linear Accelerator

The linear accelerator utilized for treatment planning was the Trilogy equipped with the Millennium Multi leaf Collimator by Varian Medical Systems. It is able to deliver beams of electrons and photons. Only the photon beam is used in this study for all cases with energies of 6 MV, 15 MV and 18 MV. There are 120 leaves total with 40 leaf pairs in the center and 10 pairs on each side. The center leaf width is 5 mm projected at isocenter, while the outer leaves are larger at 10 mm. The maximum leaf speed is 2.5 cm/s. The treatment planning system was the external beam planning system of Eclipse (Version 10.0.28.2, Varian Medical System) and the volume calculation used was the Anisotropic Analytical Algorithm (AAA, version 10.0.28.2). The Progressive Resolution Optimizer (PRO) utilized in the RapidArc optimization was Version 10.0.28.2. Varian's Leaf Motion Calculator (version 10.0.28.2) was enabled for the IMRT leaf sequence generation (see Fig.2.1).

A.2. CT simulation

It is necessary for each cancer center to have CT simulator in the radiation therapy department [28]. CT planning with virtual simulation is a feasible and useful tool in the treatment planning for patients with breast cancer undergoing curative postoperative RT. Although it is associated with a slight increase in the treatment cost, which provides many advantages. These include a greater precision in localization of target tissue and organs at risk, better evaluation of the volume and dose received by organs at risk and greater accuracy in breast boost irradiation. These advances hopefully will lead to an improvement in treatment precision, planning and treatment efficiency and

consequently translate into better tumor control probability and reduced treatment-related normal tissue complication probability[29]. The CT scanner couch should be flat and comfortable for the patient and compatible with the therapy machine couch. The positioning of laser lights in the CT room must be similar to those in the treatment room to ensure exact positioning of the patient (see Figure.2..2).In this study, the patients underwent pervious computed tomography simulation (CT-sim) (GE Light Speed 16 Slice CT) for treatment planning. For all patients, plans were designed on CT scans acquired 5 mm slice thickness, except for head and neck cases that acquired 2 mm slice thickness, and included the region of interest. The patients were positioned supine and straight and level. The contours that were generated were the Gross Tumor Volume (GTV), Clinical Tumor Volume (CTV), Planning Target Volume (PTV), ipsilateral lung, contralateral lung, contralateral breast, heart, spinal cord and body. The GTV which is the gross tumor volume is the total lumpectomy cavity which can be identified with the help of surgical clips placed at the time of surgery. The CTV was defined by the three dimensional uniform 1.5 cm margin expanded in all directions around the GTV, however this volume was constrained to lie 5 mm within the external contour and up against the major muscle. The PTV volume was defined to lie within the radio-opaque wire kept during CT simulation as deep as the anterior chest wall muscles. The lungs and external surfaces contoured using semi-automatic contouring techniques. The CTV, PTV, and Organs at Risk (OARs) were generated in accordance with the Radiation Therapy Oncology Group (RTOG) 0319 protocol.12

B. Planning technique

After simulation, the CT images were transferred to the External Beam planning system of Eclipse using 6 MV and 15 MV photon beam data. The Progressive Resolution Optimizer (PRO) was used for the RapidArc plans. The Anisotropic Analytical Algorithm (AAA) was used for photon dose calculation for all cases. For RapidArc, arcs were used clockwise (181˚- 179˚) and anticlockwise (179˚- 181˚), the collimator was rotated 30˚ to 330˚ with the dose rate varied between 0 MU/min and 600 MU/min (upper limit) to reduce the effect due to inter-leaf leakage. The double arc technique was expected to achieve better target dose coverage than the single arc because the independent optimization of two arcs allows each arc to create a completely unrelated sequence of MLC shapes, dose rates and gantry speed combinations. For the 3D-CRT plans, all of the gantry angles and numbers of radiation fields (range, 3-4) were manually selected on the basis of the formalism relationship between the PTV and OARs to cover at least 95% of the PTV and spare the OARs. The dose rate of 400 MU/min was used for 3D-CRT. Wedges

were used to provide a more homogenous distribution. The optimization constraints for OARs using RapidArc are illustrated in Table.2.1.

C. Compile Patient Database

C.1. Patient selection

Institutional Review Board (IRB) approval was obtained before the initiation of this retrospective study. The plans of 6 different malignant tumor patients who had received radical RapidArc treatment from 2012 to 2014 at KAMC were randomly selected and re-planned for 3-dimensional conformal radiation therapy. The sample included d female patients only and the median age was 54 years old (range, 47 - 57 Years).

C.2. Patient Anonymization

Patient names, age, sex, treatment site, treatment modality and codes were collected and recorded in an Excel sheet. Each patient was assigned a research code of 0xx, where xx is a number from 01 to 06. The patient's last name and medical record number were replaced by this research code, and all other personal information was removed. Furthermore, the personal information in the image set header files was removed. Table 2, lists the cases used for this study, indicating their age, sex, treatment site and modality. A malignant neoplasm is composed of cells that look less similar to the normal cell of origin or an abnormal mass of tissue arising from an abnormal proliferation of the cells. Malignant neoplasms derived from epithelial cells are called carcinomas, which is a cancer that begins in the skin or in tissue that cover body organs. Those derived from mesenchymal (connective tissue) cells are called sarcomas. Invasion breast carcinoma is group of malignant epithelial tumor characterized by invasion of adjacent tissue and a marked tendency to metastasize to distant sites [30].

D. Treatment Plan Evaluation Metrics

D.1.Dosimetric Plan Evaluation Metrics

The dosimetric evaluation metrics used to compare the two plans, in terms of mean, maximum and minimum doses to PTV, were dose to 95% of PTV, Homogeneity Index (HI), Conformity Index (CI), Target Coverage Index (TCI) and Mean and maximum doses to critical organs and normal tissue. The dose to 95% of the PTV (D95%) was used to quantify PTV coverage. The homogeneity index (HI) was used to evaluate uniformity (homogeneity) of dose

within the PTV and is calculated as

$$\mathbf{HI} = \frac{D_5}{D_{95}} \qquad \mathbf{(1)}$$

Where D_5 and D_{95} represent the dose delivered to 5% and 95% of the PTV, respectively. The smaller and closer the value of HI is to 1, the better the homogeneity of the PTV[31]. The conformity index (CI) was also calculated and can be defined as the degree of conformity of the plans, which is a ratio of the PTV receiving 95% of the prescribed dose divided by the volume of the PTV. A CI value approaching 1 indicates a higher degree of conformity.

$$\mathbf{CI} = \frac{PTV_{95\%\,PD}}{V_{PTV}} \qquad \mathbf{(2)}$$

The target coverage index (TCI) accounts for the exact coverage of PTV in the treatment plan at the prescribed dose as shown below:

$$\mathbf{TCI}= \frac{PTV_{PD}}{PTV} \qquad \mathbf{(3)}$$

Where PTV_{PD} is the PTV coverage at the prescribed dose (PD) and PTV is the volume of PTV. Target conformity index reports target dose coverage as a value between 0 and 1. A value of 1 indicates an ideal plan with target coverage by prescribed dose. However, a TCI value of 0 indicates the whole target volume is not covered by the prescribed dose [32-34].

D.2. Breast cancer

The most common type of breast cancer that forms in tissue of the breast is ductal carcinoma, which begins in the lining of the milk ducts (thin tubes that carry milk from the lobules of the breast to the nipple). Another type of breast cancer is lobular carcinoma, which begins in the lobules (milk glands) of the breast. Invasive breast cancer is breast cancer that can be spread from where it began in the breast ducts or lobules to surrounding normal tissue. Breast cancer occurs in both men and women, although male breast cancer is rare [35]. The breast cancer has increased globally over the last several decades [36-38]. The highest increase of the breast cancer has been detected in Asian countries [39]. With women at edge fortied whereas at USA, and Europe, women with breast cancer at edge sixties. In India premenopausal patients constitute about 50% of all patients [40]. It is expected that in the coming decades, these countries would account for majority of new breast cancer patients diagnosed globally. Over 100,000 new breast cancer patients are estimated to be diagnosed annually in India[41]. Radiotherapy is an integral part of breast cancer management after Breast Conservative Surgery (BCS) in early stage breast cancer. Survival

rates are similar for BCS with adjuvant Radiotherapy (RT) and mastectomy for early stage breast cancer and Breast Conservative Surgery (BCS) is known as a gold standard[42-44]. Six patients of breast cancer who's received 60 Gy in 30 fractions were discussed in this study. The median age was 48 years with ringed from 27 to 60 years. CT Scans with 0.5 cm slice thickness obtained extending from the hyoid bone to the upper abdomen, including both breast, bilateral lungs and the heart. After CT scan, the images transferred to planning system (TPS). 3D-CRT plan was used two parallel opposing tangential, which allows acceptable coverage of the breast tissue while minimizing the dose to the adjacent critical structures, physical or dynamic wedges are usually added to these tangential beams in order to compensate for the rapid changes in external contours and to improve the dose uniformity to the entire breast , using 6 MV photon and dose rate 400 MU/min (see Figure.2.3)[45].RapidArc plan was used two arcs clockwise (181˚- 65˚), the collimator was rotated 30˚ to 330˚, using 6 MV photon and dose rate 600 MU/min (see Figure.2.4). RA and 3D-CRT details for each patient as prescribed dose, number of fractions, dose per fractions, PTV volumes and number of fields or arcs are given in Table 3 and dose constraints adopted by the physician for the organs at risk are given in Table.2.2.

3. Results

Differences were recorded between those patients who planned with 3D-CRT and those who planned with RapidArc. Thus one patient was selected to represent all other patients in this site for isodose distribution comparison, dose volume histogram (DVH) comparison, dosimetric results for the PTV and dosimetric results for the critical organs . DVHs figures include the PTV and critical organs for each modality and show the percentage of the total volume (y-axis) of each ROI receiving a specified dose (x-axis) in units of Gy (table.2.1). Lungs had dose constrains corresponding to the V20Gy, V10Gy and V5Gy shown in table 3.5. The upper and lower limits on the PTV were set to 107% and 95% of the prescribed dose respectively. The representation of patient's prescription doses, PTV volume and field for 3DCRT and RA, given in table.3.1

A. PTV

A statistically significant difference between RapidArc and 3D-CRT in the mean dose to the PTV ($p < 0.002$) has been observed (Table.3.2). The mean value of the PTV was 51.38 ± 2.172in RapidArc and 52.21 ± 1.963in 3D-CRT. The maximum dose to the PTV in RapidArc (62.90 ± 2.867) and in 3D-CRT (60.70 ± 2.887) had a lower

maximum dose to the PTV (p = 0.011). This results indicates that RapidArc was better than 3D-CRT. The average minimum dose in RapidArc was (34.33 ± 3.973) compared to (27.15 ± 13.273) in 3D-CRT, (p = 0.160). The dose to 95% of the PTV was (46.50 ± 2.593) in RapidArc to (46.35 ± 2.46) in 3D-CRT, (p = 0.588). Conformity index (CI) was approximately equal in both modalities with an average value of (0.014 ± 0.005) in RapidArc compared to (0.029 ± 0.008) in 3D-CRT, (p = 0.000). The average homogeneity index (HI) in VMAT was 1.064 ± 0.019 to 1.091 ± 0.019 in 3D-CRT, (p = 0.000). Therefore, RapidArc achieved an improvement in HI. Target coverage index (TCI) in RapidArc was (0.006 ± 0.003) and (0.008 ± 0.006) in 3D-CRT.

A.1. Patient-002

Patient-002 was a 60-year-old woman diagnosed with malignant neoplasm of other specified sites of female right breast. After receiving curative dose by RapidArc, 3D-CRT plan was done for the comparison.

A.2. Isodose Distribution Comparison

Isodose distributions for the RapidArc (see Figure.3.1A) and 3D-CRT (see Figure.3.1B) plans were shown below. The 3D-CRT plan contained the PTV receiving greater than 103% of the prescription dose, 61.8 Gy, RapidArc plan the PTV receiving greater than 106% of prescription dose, 63.6 Gy. The dose distribution within the PTV was homogeneous in the both modalities. There were hot area (doses greater than 61 Gy) in the medial portion of the PTV in the 3D-CRT plan and the RapidArc plan. The distributions showed comparable PTV dose coverage between the two modalities. TV conformity in the 3D-CRT plan was better than in the RapidArc. There was a small region of the PTV in the RapidArc plan receiving 63 Gy or greater, resulting in what appeared to be greater PTV dose conformity in the 3D-CRT plan.

A.3. DVH Comparison

DVH provides useful quantitative dose assessment by direct visual inspection of the dose curve [18]. (See Figs.3.2, 3.3, 3.4,3.5 and 3.6) for lung, spinal cord, PTV and all critical organs contains a DVH for the RapidArc and 3D-CRT plans for patient-002. The y-axes of a DVH, specifically for the PTV, represent the region where the curve bends away from 100% and “falls off” with the curve maintaining a constant slope. The RapidArc plan contained a broader region in the PTV, which indicates higher dose coverage compared with 3D-CRT. The PTV had a sharper falloff in the RapidArc plan representing the superior PTV dose homogeneity observed in the isodose distributions. DVHs

showed a higher dose to right lung in the3D-CRT plan comparable to that of RapidArc plan. The dose homogeneity within the PTV as seen in the isodose distributions was high in 3D-CRT.

A.4. PTV-002

Results for the PTV are shown in Table 3.2. The RapidArc plan showed better dose-metric results in the PTV in almost every metric for patient-002. The RapidArc plan achieved lower mean dose to the PTV and higher maximum dose. PTV dose coverage, as measured by the minimum dose and the dose to 95% of the volume, was higher in the RapidArc plan. There was very little difference in the homogeneous dose distribution in the PTV between RapidArc and 3D-CRT, achieving a HI of 1.23 in RapidArc plan and 1.24 in the 3D-CRT plan as shown in table.3.3 . However, the RapidArc plan was slightly lower CI and TCI than 3D-CRT as shown in table 3.4.

A.6. Organs at risk (OARs)

Table 3.5 shows the results for the right lung. The mean and maximum dose was lower in RapidArc. The maximum dose and V20Gy in the lungs were lower in the RapidArc plan. 85.4% of the lungs received at least 5 Gy in the RapidArc plan, while only 36.6% received this dose in the 3D-CRT plan. Similarly, 32.1% of the lungs received greater than 10 Gy in RapidArc, while only 27.9% received this dose in 3D-CRT.

4. Discussion

Many studies on comparison of dose distribution for breast cancer radiotherapy techniques have been reported [46, 47]. In the current study, we reported a dosimetric comparison between the two techniques of right-sided breast cancer. Comparison was performed by dose-based analysis on PTV range and critical organs. CI, HI and TCI were calculated as shown in Table 7. Nearly all of the dosimetric planning goals were met in the VMAT plans for each of the 6 patients in this study and are explained individually . Several studies have found that the use of two arcs resulted in better plan quality than using one. Additionally, two arcs were used based upon clinical experience with breast planning in King Abdullah Medical City (KAMC), where a single arc was found to be insufficient to achieve dose constraints. VMAT plan had a better homogeneity index (HI) and target coverage index (TCI) with the PTV and equivalent conformity index (see Figure.4.1A, Figure.4.1B and Figure.4.1C). Conformity index reports target dose coverage as a value between 0 and 1. A value of 1 indicates an ideal plan with target coverage with no

over/under-dosage of target sub-volumes, a CI value of 0 indicates the whole target volume is not covered by the therapeutic dose or the existence of a severe cold spot(s) in the target . Figure.4.1A indicates that there were no significant differences in the conformity between the two modalities. The values of 3D-CRT were lower than VMAT, which is an indication of the improvement of the conformity in VMAT modality. This finding is consistent with pervious study that found VMAT capable of superior PTV conformity in breast treatment plans. An HI with a value close to 1 indicated better homogeneity. Figure.4.1B illustrates the homogeneity index for both modalities, with VMAT plans showing significantly better PTV homogeneity. Additionally, TCI with a value close to 1 indicated relatively better target coverage. Figure.4.1C shows the disparity in values between the two modalities, where the values of TCI were higher in some cases and lower in others. This is due to target coverage by prescribed dose, where a value of 0 indicates that the target volume is not covered by the prescribed dose. However, not all treatment plans were able to successfully meet each OAR dose constraint due to the close proximity of the PTV, while dose tolerance to critical structures was still maintained. VMAT achieved a better mean dose to central OARs: lung and heart. The lower OAR doses of VMAT were achieved leads to increase the mean dose to normal breast. It is important to note that the normal breast was not defined as an OAR in our study. In most cases, the minimum and maximum doses to the PTV were better in the VMAT plans. The results outside of the PTV were mixed. In regard to D95%, there was no significant difference in PTV coverage. A disadvantage that we detected in the VMAT planning technique was the increased time required for planning. Based on our results, VMAT's advantages, including tumor coverage, improved OAR sparing and significant reduction of delivery time are well worth the extra time needed for planning. VMAT is technically more advanced, while 3D-CRT has the ability to deliver the appropriate dose to the target. The main benefit of VMAT over 3D-CRT is the ability to optimize the treatment in the planning stage to deliver the appropriate dose to the target while optimizing the plan to adhere to the OAR constraints. The findings of our study show that VMAT allowed a better reduction of dose in OARs, particularly the OAR for which dose was not optimized and might receive a higher dose. This could occur because during VMAT, a larger body part is typically irradiated with a small dose, and not all OARs can be taken in to the optimization process. In the present study, the maximum dose to the right lung was higher than left lung. Generally, the critical structure in the right side received a higher dose than left side, due to the position of the tumor. From pervious study, VMAT improved the plan conformity compared to 3D-CRT [48],in which the mean dose to the right lung with VMAT, lower than the mean dose to the right lung with 3D-CRT planning by almost 7 Gee while V20Gy reduced with VMAT by 19%

compared with 3D-CRT planning . The low doses < 10 Gee were also reduced by 21.9% with VMAT planning compared to 3D-CRT, and VMAT was lower in the V5Gy by almost 6%. Our study has not fully agreed with this result, the mean dose was lower in VMAT by 2 Gy and reduced the V20Gy to 11 Gy, while V5Gy and V10Gy was lowered with 3D-CRT by 49 Gy, 5 Gy respectively. One study observe that VMAT has been revealed to deliver lower doses to the ipsilateral breast and lung and offer better dose conformity than 3D-CRT technique for partial breast irradiation patients[49, 50]. Until now we found that the use of VMAT in breast cancer achieve better results and spare the healthy tissue more than 3D-CRT.

5. Conclusion

Breast cancer was treated with three dimensional conformal radiation therapy in 6 patients. 3D-CRT resulted in poor dose conformity to the target and high doses to critical organs in some cases. Volumetric modulated arc therapy is a relatively new treatment technology that provides better conformity to the tumor, sparing healthy structures and better low-dose OAR sparing in the lungs and heart. This study has also shown that VMAT is superior to 3D-CRT in term of PTV, conformity and homogeneity, but not in terms of doses to critical organs in some cases. Clinical preference for accepting the VMAT class solution over 3D-CRT treatment was preferred to be determined on a case by case basis. VMAT will be the treatment of choice for breast tumors requiring PTV conformity and homogeneity that VMAT provides. This study suggests that VMAT class solution is the superior treatment option. The major advantage of VMAT over 3D-CRT is the shorter treatment time. In conclusion, due to the ability of VMAT to generate highly conforming and efficient treatment plans that are clinically comparable to 3D-CRT, the results of this study suggest that VMAT be considered as a viable option for the treatment of various sites of tumors.

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Competing interests

"The authors declare that they have no competing interests."

Authors' Contributions

Alleghany participated in the diametric evaluation metrics and participated in comparing the two plans in terms of mean, maximum and minimum doses to PTV, Homogeneity Index (HI), Conformity Index (CI), Target Coverage Index (TCI) and mean and maximum doses to critical organs and normal tissue and drafted the manuscript. Aida R participated in measurements of the dose to 95% of the PTV (D95%) to quantify PTV coverage and the homogeneity index (HI) to evaluate uniformity (homogeneity) of the dose within the PTV and participated in drafted the manuscript. Huda A participated in the design of the study and performed the statistical analysis and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript and H. S. Ibrahim participated in the dosimetric evaluation metrics.

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Figure Legends

Figure.2 .1 LINAC machine and MLC.

Fig.2.2 CT scanner

Figure.2.3 3D-CRT plan setup for breast cancer using two fields.

Figure.2.4 RapidArc plan setup for breast cancer using two arcs and gantry angles range.from (181˚- 65˚).

Figure.3.1 Isodose distributions for patient-002 showing (a) RapidArc and (b) 3D-CRT.

Figure.3.2 Comparison of DVHs between RapidArc (triangles) and 3D-CRT (squares)Planes, for left lung.

Figure.3.3 Comparison of DVHs between RapidArc (triangles) and 3D-CRT (squares) Planes, for Right lung.

Figure.3.4 Comparison of DVHs between RapidArc (triangles) and 3D-CRT (squares)Planes, for both lungs.

Figure.3.5 Comparison of DVHs between RapidArc (triangles) and 3D-CRT (squares)Planes for Spinal Cord.

Figure.3.6 Comparison of DVHs between RapidArc (triangles) and 3D-CRT squares)Planes for all critical organs . The PTV in red color.

Figure.4.1 A histogram plot of (CI) for 6 breast cases (A), A histogram plot of (HI) for 6 breast cases (B) and A histogram plot of (TCI) for 6 breast cases (C) .

Figures

Figure.2. 1

Figure. 2.2

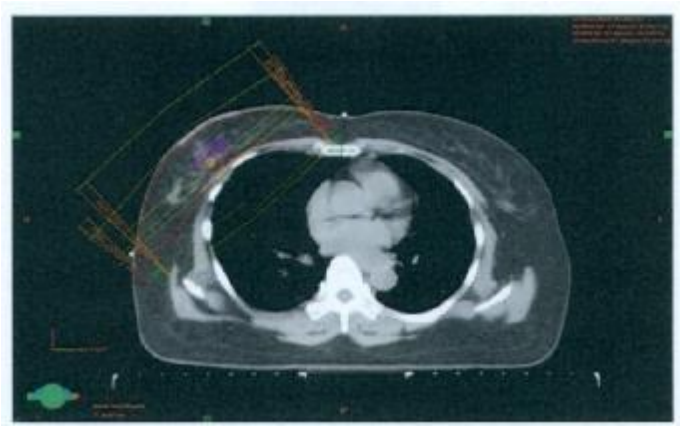


Figure. 2.3

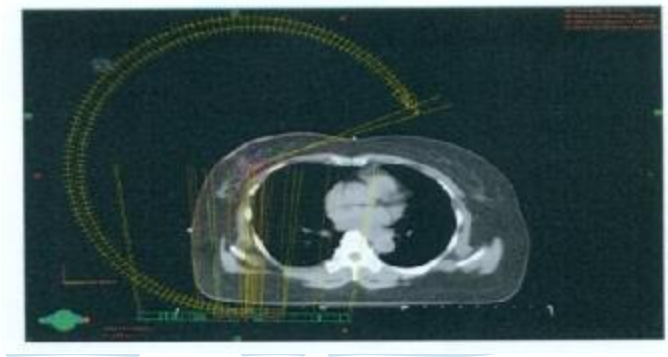
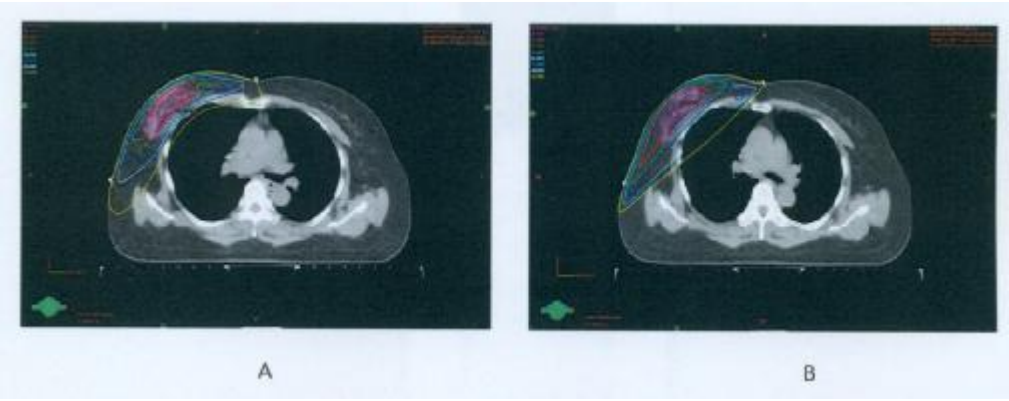


Figure.2.4



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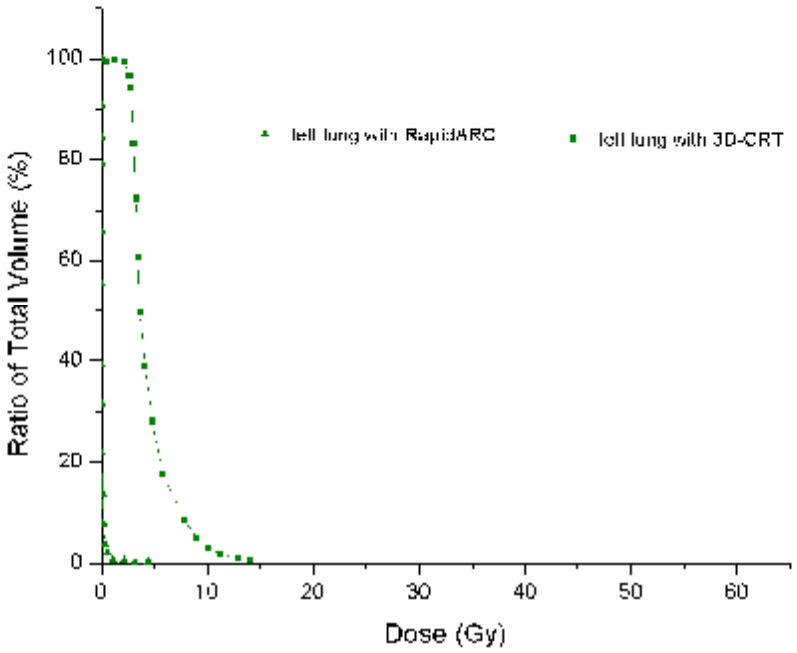
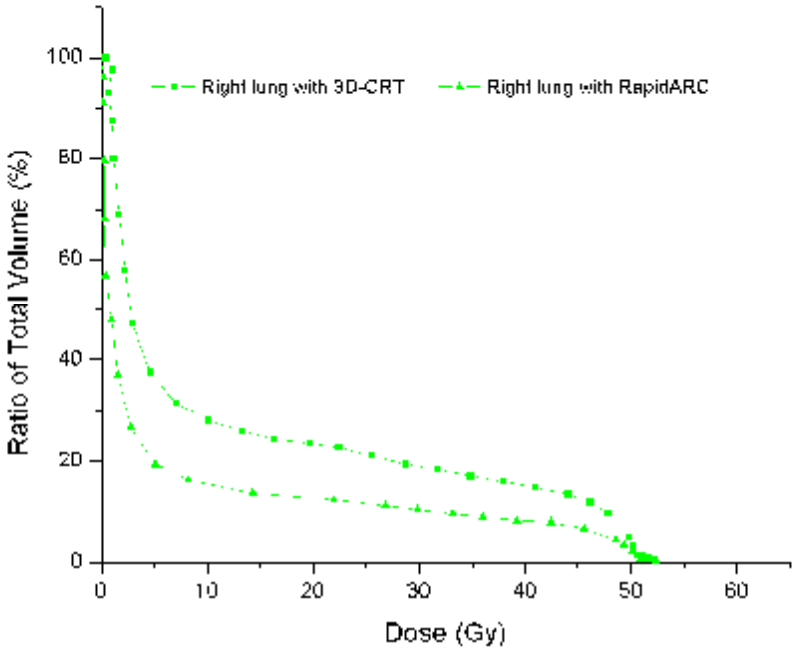


Figure.3.2



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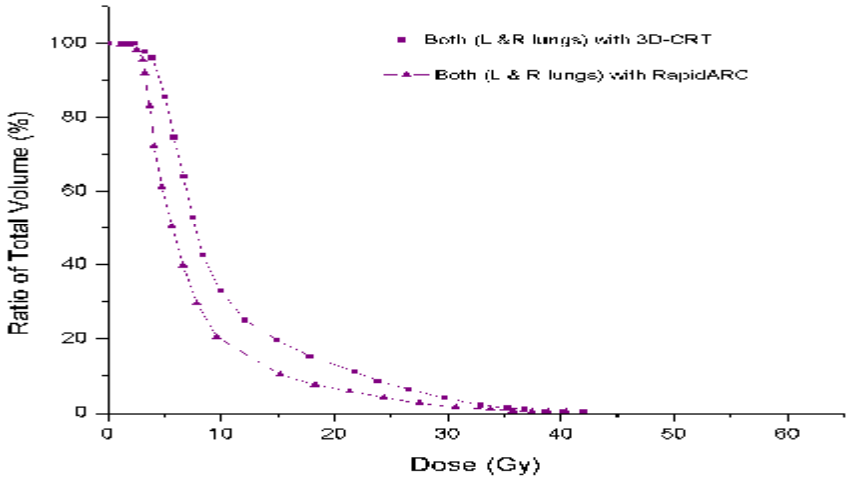
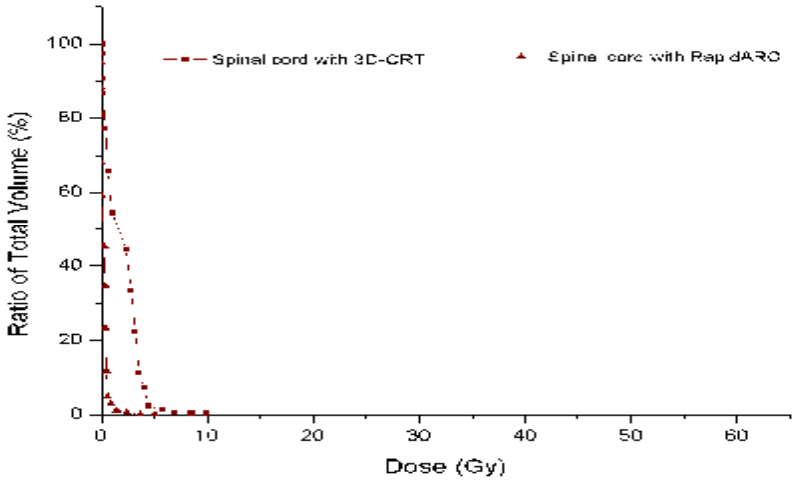


Figure.3.4



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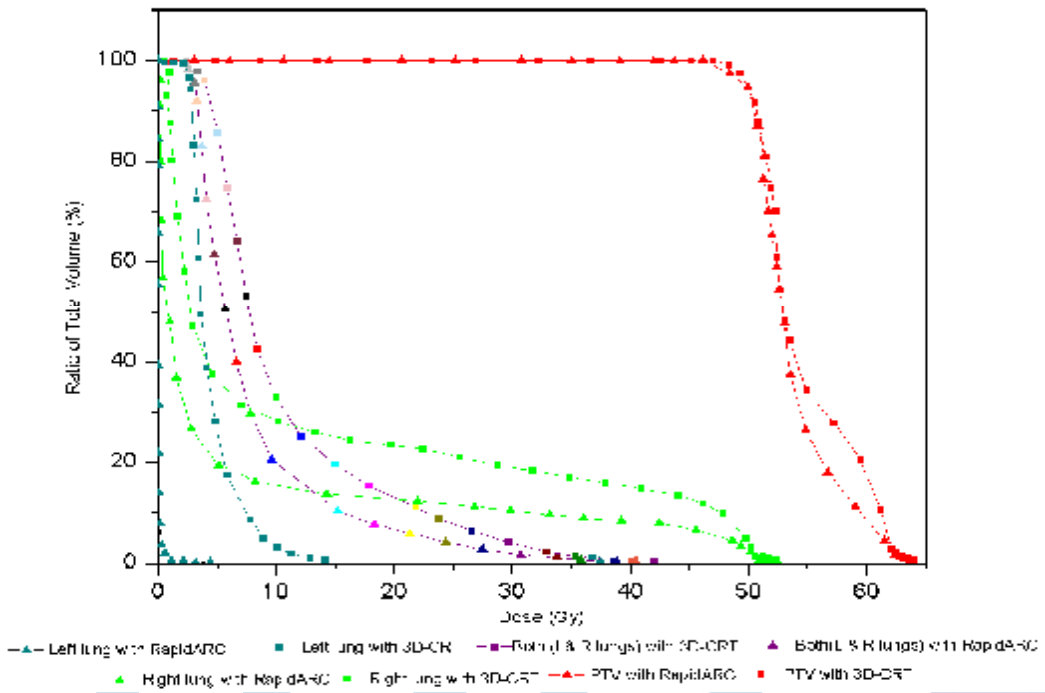
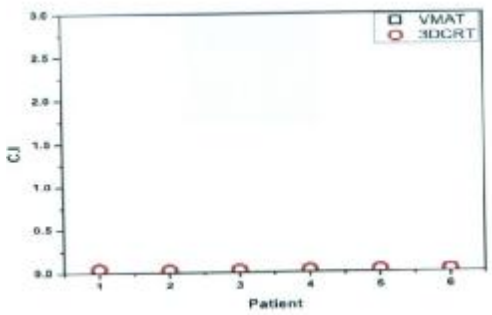
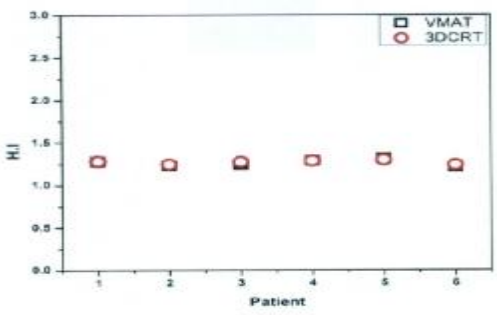


Figure.3.6



A



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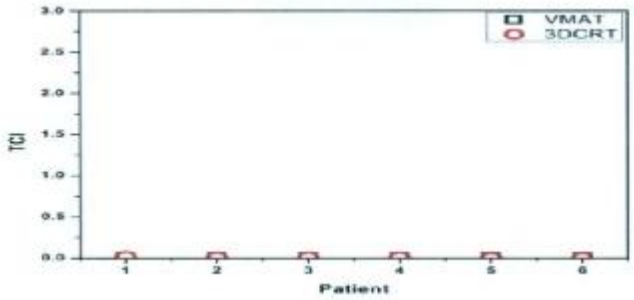

C

Figure.4.1

Tables and captions

Table.2.1. The dose constraints of organ at risk.

Critical organ at risk	First Criteria : Ideal	Second Criteria : Acceptable
Brainstem	Point ≤54 Gy	Point & 1% volume < 60 Gy
Spinal cord	Point < 45 Gy	Point & 1mL volume< 50 Gy
Optic chiasm	Point < 54 Gy	Point & 1% volume < 60 Gy
Optic nerve	Point < 54 Gy	Point & 1% volume < 60 Gy
Lens	Point < 6 Gy	Point & 1% volume < 10 Gy
Eyeball	Point < 50 Gy	Mean < 35 Gy
Heart	Mean < 26 Gy V30< 46%	----------
Lung	V20≦ 30%	----------
Liver	Mean < 30-32 Gy	----------
Kidney	Mean < 15-18 Gy	----------

Table. 2. 2. Patient database (Malignant neoplasm).

Patient Code	Sex	Age	Treatment site	Modality
001	F	54	Malignant neoplasm of upper quadrant of female breast	RA – 3DCRT
002	F	60	Malignant neoplasm of specified sites of female breast	RA – 3DCRT
003	F	27	Malignant neoplasm of specified sites of female breast	RA – 3DCRT
004	F	57	Carcinoma in situ of breast	RA – 3DCRT
005	F	39	Malignant neoplasm of specified sites of female breast	RA – 3DCRT
006	F	52	Malignant neoplasm of specified sites of female breast	RA – 3DCRT

Table.3.1. Representation of patients' prescription doses, PTV volume, and number of fields for both 3D-CRT and RA.

Patient Code	PD(Gy)	No of Fraction	Dose per Fraction	PTV(cm^3)	No of Field/Arcs	
					RA	**3D-CRT**
001	60	52.56	30	1.8	1052.2	2 fields
002	60	60	30	2	838	2 fields
003	60	60	30	2	884.9	2 fields
004	60	60	30	2	985	2 fields
005	60	60	30	2	750.5	2 fields
006	60	60	30	2	984.5	2 fields

Table.3.2. Evaluation metrics for PTV in terms of .D_{MEAN} , D_{MAX} and D_{MIN} covered 95% of the target.

Patient Code	D_{mean}(Gy)		D_{max}(Gy)		D_{min}(Gy)		$D_{95\%}$(Gy)	
	RA	3DCRT	RA	3DCRT	RA	3DCRT	RA	3DCRT
001	47.1	48.3	57.5	54.9	30.7	5.3	42.1	41.7
002	52.6	53.2	63.4	61.8	40.5	38.0	48.6	48.5
003	52.7	53.4	62.9	62.5	33.0	19.0	47.9	47.4
004	52.1	53.1	64.7	62.4	36.5	34.1	46.7	47.0
005	51.2	52.2	65.8	61.3	29.9	26.3	44.9	45.7
006	52.6	53.1	63.1	61.3	35.6	40.2	48.8	47.8
Mean	51.38 ± 2.172	52.21 ± 1.963	62.9 ± 2.867	60.70 ± 2.887	34.33 ± 3.973	27.15 ± 13.273	46.5 ± 2.593	46.35 ± 2.461
P-value	**P < 0.001**		**P < 0.011**		**P < 0.160**		**P < 0.588**	

Table3.3. Evaluation metrics for the PTV in terms of CI, HI and TCI.

Patient Code	CI = $\frac{PTV_{95\%FD}}{V_{PTV}}$		HI = $\frac{D_5}{D_{95}}$		TCI = $\frac{PTV_{FD}}{PTV}$	
	RA	**3DCRT**	**RA**	**3DCRT**	**RA**	**3DCRT**
001	0.0239	0.0467	1.2808	1.2840	0.0124	0.0185
002	0.0160	0.0300	1.2344	1.2466	0.0064	0.0102
003	0.0132	0.0258	1.2477	1.2749	0.0047	0.0093
004	0.0115	0.0266	1.2887	1.2882	0.0057	0.0083
005	0.0097	0.0261	1.3131	1.2980	0.0054	0.0017
006	0.0108	0.0237	1.2120	1.2366	0.0029	0.0025
Mean	0.014 ± 0.005	0.029 ± 0.008	1.262 ± 0.037	1.271 ± 0.024	0.006 ± 0.003	0.008 ± 0.006
P-value	**P < 0.000**		**P < 0.246**		**P < 0.202**	

Table.3.4. Evaluation metrics for the PTV – patient-002**.**

Parameter	Objective	RA	3D-CRT
Mean (Gy)	60	52.6	**53.2**
D_{max} (Gy)	64.2	63.4	**61.8**
D_{min} (Gy)	54	40.5	**38.0**
$D_{95\%}$	7	48.6	**48.5**
Conformity Index (CI)	1	0.016	**0.030**
Homogeneity Index (HI)	1	1.234	**1.246**
Target Conformity Index (TCI)	1	0.0064	**0.0102**

Table .3.5. Evaluation metrics for the OARs – patient-002.

Organ	Parameter	Objective	RA	3D-CRT
RT. lung	Mean (Gy)	Minimize	10.4	**12.0**
	V_{5Gy}	No more than 50% of the lung for right-sided cancer	85.43	**36.66**
	V_{10Gy}	No more than 35% of the lung for right-sided cancer	32.12	**27.91**
	V_{20Gy}	No more than 15% of the lung for right-sided cancer	12.45	**23.26**