Journal of Radiation and Nuclear Applications
An International Journal

http://dx.doi.org/10.18576/jrna/110110

Bilateral kidney sparing in treatment of pancreatic malignancies by VMAT vs. IMRT strategies using Real Time Tumor Tracking System

Wafaa Rashed [1], Rania Abdelrahman[2,], Hany El-Gamal[3], Mostafa Abd el-wanis[4], Khaled. M. El-Shahat [*5]*

[1]Physics Department, Faculty of Science, New Valley University, 72511, El-Kharga, Egypt.
[2]Assuit Military Center for Radiotherapy, Assiut ,Egypt.
[3]Technology of Radiology and Medical Imaging Department, Faculty of Applied Health Sciences Technology, Menoufia University, 32951, Menoufia, Egypt.
[4]Radition Oncology Department, South Egypt Cancer Instuite, Assuit University, 172526 Assuit, Egypt.
[5]Department of Medical Physics, Al Azhar University, Cairo, Egypt.

Received: 30 Aug. 2025, Revised: 20 Oct. 2025, Accepted: 30 Nov. 2025
Published online: 1 Jan. 2026

Abstract: A dosimetric study was conducted to compare two high-intensity modulated treatment planning strategies (Volumetric Modulated Arc Therapy (VMAT) and Intensity Modulated Radiotherapy (IMRT)) for pancreatic malignancies. The study incorporated a Real-Time Tumor-Tracking Radiation Therapy (RTRT) system to enhance treatment precision. Its primary goal was to evaluate which technique provides superior tumor dose coverage and early tumor response while minimizing severe radiation toxicities to organs at risk (OAR), particularly for bilateral kidney preservation. This dosimetric analysis was performed in 30 patients who had undergone radiotherapy for pancreatic carcinoma at our institution. We compared 9-field IMRT and 2 arcs RapidArc (RA) plans for each patient of 30s. Each treatment plan was designed in such a way that standard fractionation consists of 1.8 Gy daily fraction in 28 fractions to deliver a total dose of 50.4 Gy to the planning target volume (PTV). Treatment planning objectives were ensuring that 95% of the PTV received ≥ 95% of the radical prescribed dose and no more than 2% of the PTV received more than 107%; this involves assessing treatment plans using metrics like dose-volume histograms (DVH), homogeneity index (HI), and conformity index (CI) to obtain the optimum strategy as appropriate for the treatment of pancreatic cancer. The DVH for each IMRT & RA plans in terms of the target volume and the radiosensitive organs (right and left kidneys) were compared, in addition to the monitor units (MUs) and delivery treatment time, which were also reported. All of these comparative plans achieved the treatment plan objectives as D95% for IMRT = 48.9 Gy and for RA = 48.6 Gy, while RA exhibited superiority in protecting bilateral kidneys from the probability of injury as it decreased the mean tolerance dose irradiated to both kidneys (for the left kidney: the RA D_{mean} (4.5-5.2) Gy vs. (9.2-10.5) Gy in the IMRT plans; for the right kidney: the RA D_{mean} (3.4-4.1) Gy vs. (8.2-9.1) Gy in the IMRT plans). The results provide evidence of potential benefits of RapidArc with real-time tumor-tracking in pancreatic carcinoma treatment, as RA allows significant dose reduction for bilateral kidneys while enhancing dose conformity, improving targeting accuracy, and reducing treatment time and monitor units.

Keywords: Pancreatic Cancer, IMRT, VMAT, Real-Time Tumor-Tracking System, Conformity index, Homogeneity index.

1 Introduction

Pancreatic cancer arises when cells in the pancreas, a yellow-tan lobulated glandular organ seemed as a thin pear, begin to multiply out of control and form an abnormal mass (tumor); these cancerous cells have the ability to invade other body organs [1]. There are two types of pancreatic cancer. The most common type is the pancreatic ductal adenocarcinoma (PDAC), accounts for about 90% of cases [2], which occurs in exocrine pancreas cells that produce digestive enzymes that help food to break down into substances that the body can use. While the other small minority of pancreatic cancer type is pancreatic neuroendocrine tumors (PanNETs), which occur in endocrine pancreas cells that produce hormones, such as insulin and glucagon, which manage blood sugar levels and

*Corresponding author e-mail: khalid khelshahat@yahoo.com

help the body to use and store the energy that it can get from eating food. The term "pancreatic cancer" is sometimes used to refer only to pancreatic ductal adenocarcinoma [3]. The tumor removal surgery is the most effective cure for pancreatic cancer, while palliative surgery may be used to remove sources of pain and increase quality of life. Furthermore, additional treatments including radiation therapy, chemotherapy, and chemo-radiation therapy can also be options for pancreatic cancer treatment according to the tumor stage and overall health of the patient. If radiotherapy is the pancreatic cancer treatment option, the surrounding normal organs are subjected to be affected by the radiation beam during radiotherapy for pancreatic cancer; when the absorbed dose to these radiosensitive organs exceeds the tolerance dose, these organs are subjected to severe radiation toxicities.

The pancreas is surrounded by many organs; attention should be paid to all of them, especially to both kidneys, due to pancreatic cancer and kidney health have complex and reciprocal effects, as pancreatic carcinoma can spread to the kidneys, and renal cancer can also metastasize to the pancreas. Additionally, the relationship between pancreatic cancer and kidney health is multifaceted, it isn't only involving metastasis but also it can manifest with diabetes, which is a risk factor for kidney disease, including chronic kidney disease (CKD). Furthermore, there is a geographic correlation, as shown in Figure 1, between pancreatic and kidney cancers incidences, suggesting shared risk factors or pathways. So attention should be paid to control the severe radiation toxicities of both kidneys by limiting the irradiated dose to those limited dose organs during pancreatic cancer radiotherapy. The purpose of this study is to compare the morbidity, mortality, and renal allograft survival in pancreatic cancer patients during radiotherapy.

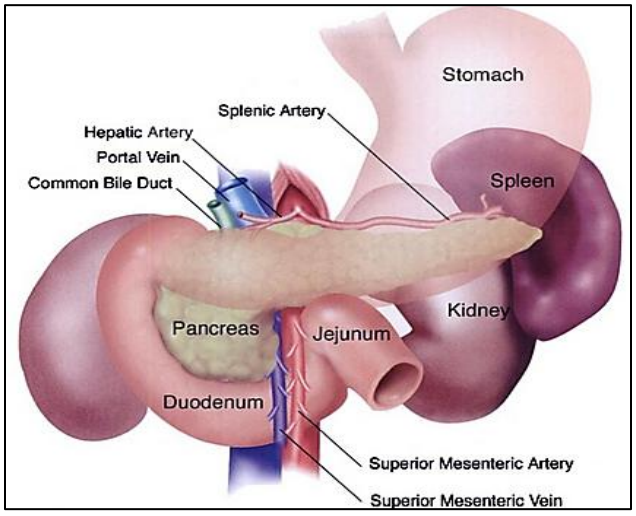


Fig. 1. Relationship of pancreas to both kidneys. [4]

Pancreatic cancer remains one of the most formidable challenges in oncology. This challenging is due to several factors, including pancreatic cancer is rarely diagnosed at its early stages. It often doesn't cause symptoms until it has already spread to other organs. Moreover, the pancreas lies in the abdominal cavity that contains a lot of vital organs that are radiosensitive organs, and exhibits motion during respiration that makes radiation therapy less accurate and increases the risk of injury to surrounding tissues during treatment. So in this study, we use two highly intensity modulated techniques (IMRT & VMAT) with the aid of a real-time tumor-tracking system to manage pancreatic motion.

Intensity-modulated radiation therapy

Intensity-Modulated Radiotherapy (IMRT) represents one of the most significant advancements in oncology over the past decade. It enables the delivery of a high radiation dose to the tumor while minimizing exposure to surrounding healthy tissues. There is a well-established correlation between the absorbed radiation dose and tumor control probability; however, the prescribed dose is often constrained by the tolerance limits of adjacent normal structures. IMRT offers superior normal tissue sparing compared with conventional techniques because of its capacity to precisely conform radiation beams to the target volume. This precision not only reduces late toxicities but also enhances tumor control and potentially improves patient survival [5].The IMRT technique employs numerous small radiation beams, each divided into hundreds of beamlets with individually modulated intensities. These beamlets are optimized to achieve improved dose conformity, particularly for complex or concave target shapes, while facilitating intentional dose inhomogeneity, tissue compensation, and dose escalation, ultimately maximizing both treatment effectiveness and safety [6-8].

There are diverse methods that have been developed to deliver IMRT such as: (i) step-and-shoot IMRT; in which small multi-leave collimator (MLC) generated segments are used and the beam is turned off when MLC leaves switching from a segment to the next one, it is also known as segmental IMRT, (ii) sliding window IMRT; in which modulated MLC velocity in multiple static radiation fields is used and the beam is on as the collimator leaves are moving continuously, it is also known as dynamic MLC-IMRT (DMLC), and More recently, techniques, (iii) volumetric modulated arc therapy (VMAT); which is a rotational form of IMRT whereby the MLC leaf positions and dose delivery rates vary during beam rotation. [9-10].

In the case of the dynamic MLC tracking delivery, there is a problem in obtaining an optimal plan and adequate coverage for all disease throughout the treatment course; due to both of tumor and patient movements, in addition to the dynamic nature of the MLC itself. Figure 2 illustrates the interplay between organ motion and leaf motion during DMLC-IMRT delivery. As the leaves of the collimator move laterally for shaping the dose to the target and a point within an organ, represented by a star, moves vertically in

response to organ motion. The two versions of the star (open and filled stars) denote two different phases of the organ motion. Depending on the phase relative to the leaf motion, the point may receive varying dose values: as the filled star does not receive any primary dose between times t_1 and t_4, and in fact it may not receive any primary dose at all, while the open star that moves upward during the same interval, receives with the full primary dose at all times.

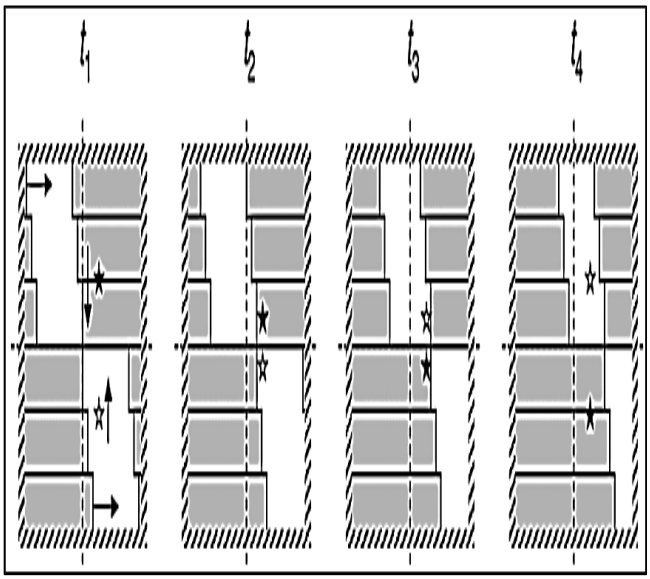


Fig. 2: Illustration of the organ motion and leaf motion interplay at IMRT with DMLC. [11]

The four dimensional (4D) treatment plans have two scenarios for taking into account all potential motions, the first scenario involves offline replanning between treatment fractions, while the second one employs online 4D treatment planning based on four dimensional computed tomography (4DCT) images. The most effective scenario integrates both respiratory phase data and real-time target position information during the treatment session, enabling adaptive plan optimization in real time.

Sawant et al. **[**12-13**]** developed a robust dynamic multileaf collimator (DMLC) tracking algorithm that was designed to manage moving and deforming targets. The algorithm acquires real-time target position data from an independent monitoring system (e.g., RPM® or Calypso®) and dynamically adjusts the MLC leaves to compensate for three-dimensional (3D) target motion. The workflow of this real-time DMLC-IMRT tracking algorithm, comprising five main steps, is illustrated in Figure 3.

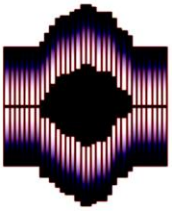
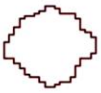
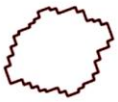
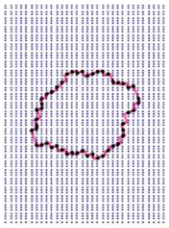
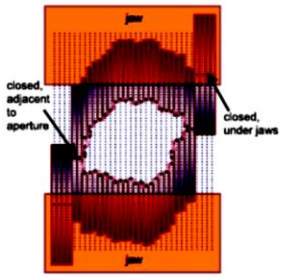
1	Read initial leaf positions from MLC file.	
2	Extract the "shape" defined by the points corresponding to MLC leaf tips.	
3	Transform this shape to match real-time target position/shape (estimated from a real-time position monitoring system).	
4	Determine the intersection points of MLC leaf trajectories with the transformed shape.	
5	Send MLC leaves to the points of intersection. Closed leaf pairs adjacent to open aperture(s) are positioned at the midpoint of nearest open leaf pair. Peripheral closed leaf pairs are sent beneath the nearest jaw.	

Fig. 3: Diagram of the workflow when tumor tracking is performed using DMLC tracking. The Figure reprinted from Sawant et al [12] is used with permission from Wiley.

Volumetric Modulated Arc Therapy

VMAT is the rotational form of IMRT, in which it can be delivered in a continuous arc during gantry rotation of the linear accelerator (LINAC) around the patient. During VMAT plan delivery, while the gantry is rotating, the beam aperture is changed continuously; also, dose rate, gantry speed, and MLC positions will dynamically vary with a 360-degree rotation of the gantry in a single or multi-arc treatment [14], so it is called RapidArc (RA). RA can commonly be used to treat head and neck cancer, whole brain cancer, esophagus cancer, lung cancer, pancreatic cancer, prostate cancer, and a wide variety of other cancerous tumor sites [15-21]. RA can mainly be delivered by two main vendors that manufacture LINACs: Elekta (Elekta Oncology Systems, Crawley, UK) and Varian (Varian Oncology Systems, Palo Alto, CA).

For organ motions, VMAT with real-time tracking must be used with potential, additional VMAT benefits such as; (i) improving targeting accuracy as RTRT can track the tumor motion during treatment that increase the delivery dose accuracy, (ii) enhancing dose conformity as RTRT can rise VMAT's ability to deliver highly modulated doses and conform it to the tumor, which resulting in potentially more sparing for surrounding healthy tissue, (iii) reducing treatment time as RTRT can shorten VMAT's treatment times, resulting in minimizing the impact of intra-fractional motion, and (iv) reducing the target volume margin as RTRT enables the gross tumor volume dose of each 4D plan (4D GTV dose) to be compared with the internal target volume dose of the original plan (3D ITV dose) [22] .

2 Experimental Sections

2.1 Study Design and Patient Populations

30 pancreatic malignancy patients were treated with IMRT using a fiducial-based real-time target tracking system and then re-planned and calculated with RapidArc plans with the aid of RTRT system. Data collection occurred over a time frame from August 2023 to May 2024. Each patient was immobilized in a supine position with arms overhead during all sessions for accurate treatment delivery. For each patient, a free-breathing treatment planning CT (Sensation Open, Siemens Healthineers, Erlangen, Germany) was used for 4D CT image acquisition with a 2 mm slice thickness. Intravenous (IV) contrast was used to visualize vessels and two kidneys. All the images were transferred from CT workstation to treatment planning system Eclipse™ (TPS, Eclipse version 15.6.03, Varian Medical Systems, Palo Alto, CA) for delineation. In general, treatment volumes should encompass primary tumor as well as regional lymph nodes. Gross target volumes (GTV) and Planning target volumes (PTV), that including (Internal Target Volume (ITV) which is clinical target volume (CTV) plus internal margin (IM), and setup margin (SM)) to account for daily setup error and motion, were designed according to the recommendation of the International Committee for Radiological Units (ICRU) report 83 [23]. OARs must be delineated using 4D data by several experienced radiation oncologist, and then confirmed by a radiologist. The irradiated dose must be calculated for each of them in all pancreas cancer sites. The fluoroscopic RTRT system has been shown to reduce translational set-up error and internal error with an accuracy of ± 1.5 mm for moving objects. Fluoroscopy should be considered at the time of simulation, verification, or 4D treatment planning to evaluate organ movement. Using 4D data; OARs such as bilateral kidneys, liver, spinal cord, stomach, and small intestine were contoured, and the irradiated dose must be calculated. Then dose-volume histograms (DVHs) should be calculated to outline the dose to target volumes and normal structures.

2.2 Planning techniques and dose constraints

The compared technique used in this study is the treated Intensity Modulated Radiotherapy plans and the retrospective VMAT plans with the RTRT system.

Treated IMRT plans

All IMRT plans were generated in an Eclipse™ TPS (TPS, Eclipse version 15.6.03, Varian Medical Systems, Palo Alto, CA). All plans were designed using a 6 MV photon beam in Flattening Filter Free mode (6 MV-FFF beam has noticeably better beam-on-time and monitor units and more dose sparing to OARs than the 6 MV-FF Flattening Filter plans [24]) in the same treatment machine of a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA) modulated by Millennium 120™ MLC, using nine coplanar sliding-window based IMRT fields with equally spaced beams arrangements (beam angles at 0°-320° every 40°) to precisely target the tumor while minimizing exposure to organs at risk. The fluence maps for each beam were imported into Eclipse and then converted to MLC sequences with MLC leaf motion calculations (Varian LMC 15.6.03). All IMRT plans were optimized on free-breathing treatment planning computed tomography images; optimization was performed using the Dose Volume Optimizer (DVO, Version 13.7.16). In plan designing, a CT image with 2 mm slice spacing and grid spacing of the dose calculation with 2 × 2 × 2 mm was utilized to calculate dose distribution using the Anisotropic Analytical Algorithm (AAA, version 15.6.03) in Eclipse considering the heterogeneity correction.

Retrospective VMAT plans

All VMAT plans were generated in an Eclipse™ TPS (TPS, Eclipse version 15.6.03, Varian Medical Systems, Palo Alto, CA). All plans were designed using a 6 MV-FFF photon beam in the same treatment machine of a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA) modulated by Millennium 120™ MLC, using a non-coplanar double-arc in opposite directions to achieve the desired dose distribution. The fluence map for a VMAT plan is generated by superposing each fluence map of the control point then imported into Eclipse and converted to MLC sequences with MLC leaf motion calculations (Varian LMC 15.6.03). All VMAT plans were optimized on free-breathing treatment planning computed tomography images; optimization was performed using the Progressive Resolution Optimizer (PRO, Version13.7.16) to optimize the arcs, beam angles, and MLC Leaf positions to optimize the dose distribution and improve target coverage while sparing surrounding healthy tissues. In plan designing, a CT image with 2 mm slice spacing and grid spacing of the dose calculation with 2 × 2 × 2 mm was utilized to calculate

dose distribution using the Anisotropic Analytical Algorithm (AAA, version 15.6.03) in Eclipse considering the heterogeneity correction.

Both a double-arc VMAT and a 9-field IMRT plan were generated for each of the 30 patients with pancreatic malignancies. The plan was designed such that standard fractionation consists of 1.8 Gy per daily fraction in 25–28 fractions to deliver a total dose of 45–50.4 Gy to the tumor bed, unresected or residual tumor, and lymph node bearing areas at risk.

Both treatment plan techniques have the same defined tumor volumes, organs at risk volumes, dose, fractionation, and optimization constraints, aimed to reduce the irradiation to OARs as much as possible while encompassing at least 95% of PTV by 95% of the prescribed dose, to explore the optimal radiotherapy planning techniques as appropriate for the treatment of pancreatic cancer and their impact on patient outcomes (i.e. the best coverage to target volume and the most sparing for organs at risk) using the real-time tumor-tracking system. In this study, we concerned in the dose irradiated to both kidneys due to the two comparative treatment techniques. The tolerance doses of the kidney were summarized in the following **table (1)**, as the mean irradiated dose to one kidney is 18 Gy, to avoid renal failure and chronic kidney diseases.

Table 1. Dose constraints for the organs at risk adhering to the local guidelines and QUANTEC [25].

OAR	Dose constraint
One Kidney	$D_{mean} \leq 18$ Gy
	$V_{12Gy} \leq 55\%$
	$V_{20Gy} \leq 32\%$

2.3 Real-time Tumor-tracking radiation therapy System (RTRT)

Both respiratory motion and organ motion influence in treatment delivery process and introduce dosimetric uncertainties. In the case of non-dynamic treatment delivery, these motions will result in dose blurring at the field edge; while in the case of dynamic treatment delivery, in addition to these motions there is the simultaneous motion of MLC leaves that also will result in the same effect. Real-time tumor tracking method is a technical development on treatment delivery as it can account for the respiration-induced motion without any beam hold. In the tracking method, the incident beam dynamically tracks the tumor motion and continuously adjusts to be aligned with the moving tumor position with the advantage of the patient's free breathing in addition to keeping treatment margins to remain small during beam delivery (100% duty cycle).

The RT-RT system is a unique Image-Guided Radiation Therapy (IGRT) system developed by *Hokkaido University* School of Medicine and Mitsubishi. Electronics Company Ltd. [26]. This tracking technique requires knowledge about the internal target motion that can be tracked during treatment delivery using specialized cameras and recorded in many different types of imagers.

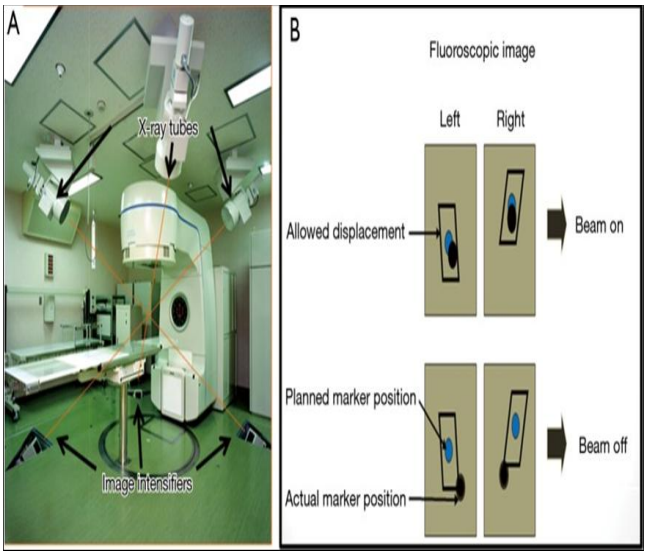


Fig.4: RT-RT systems. [27].

The RT-RT system consists of four pairs of diagnostic X-ray tube-image intensifier embedded on the floor of the LINAC room and the corresponding image intensifiers mounted on the ceiling for localization of the fiducial markers that are implanted in or close to the tumor (Figure 4A). The acquired images were in movie mode during treatment delivery for accurate tracking and dose delivery.

Real-time orthogonal fluoroscopy is repeated every 0.03 seconds. The fiducial marker is allowed to displace from its expected position for 1 to 3 mm in 3 dimensions. Beyond this tolerance, the radiation beam will be turned off automatically until the marker returns to its allowed displacement zone (area marked by the parallelogram) (Figure 2.33B). It means that the beam radiation is only delivered when the tumor is in its desired position, resulting in minimizing damage to surrounding healthy tissues.

In the current study, we investigated the safety and early tumor response of real-time tumor–tracking radiation therapy (RTRT) for 30 patients with PDAC with the aid of insertion of a fiducial marker to reduce uncertainty, which results from setup error and pancreatic motion, such as possible it can during thoracic and abdominal radiotherapy.

2.4 Plan comparison and evaluation [28]

The two planning techniques must be compared and evaluated to investigate the optimal one that is appropriate

for pancreatic cancer treatment using DVH. It is a 2D graph showing a comprehensive overview of the dose distribution within a defined volume of interest (VOI) whether it was PTV or a specific organ in the vicinity of the PTV.

DVH is displayed in the form of volume on the ordinate against the dose on the abscissa, both volume and dose can be displayed in relative (% volume and % dose) or absolute value (cc for volume and cGy or Gy for dose). There are two types of DVH; differential DVH (dDVH) and cumulative DVH (cDVH). In our study, we use cDVH in dosimetric comparisons and evaluations of the comparative plans.

The evaluated parameters for both the target volumes and radiosensitive surrounding organs can be extracted from the dosimetric data of DVH. For organ at risk, we mentioned the tolerance dose of one kidney. For target volumes, the dosimetric parameters were defined according to ICRU report 50, which are [29]:

- The maximum dose Dmax: there is a hot spot; if the value of Dmax exceeds the prescribed dose value Dp, it usually exists in the volume outside the PTV, representing how much volume receives a dose larger than 100% of the prescribed dose.
- The minimum dose Dmin: it is the lowest dose absorbed by the target volume. In contrast to Dmax, no volume limit is recommended when reporting Dmin.
- $V_{95\%}$ (the volume absorbed 95% of the dose): Optimally, 100% of the prescribed dose must cover 100% of the target volume; however, the treatment plans can be acceptable if 95% of the D_p covers 95% of the target volume [30].
- $V_{107\%}$ (the volume irradiated by more than 107% of the prescribed dose): the ICRU report 62 recommended that the Dmax in the target volume mustn't exceesds107% of the Dp as the absorbed dose in the PTV is restricted within 95% to 107 % of the prescribed dose [31].

Because of the unconventional nature of IMRT & VMAT dose distributions, especially the high degree of dose heterogeneity and fluctuations in dose as a function of position in VOI, these parameters are limited in use for such plans [32-33]. Also these parameters don't correlate well with the dose response and they are a large volume of data and can be summarized in two important evaluation indices Conformity index (CI) and Homogeneity index (HI) [34].

Conformity index (CI) [35]

It is a quantitative tool that measures the dose conformation on the target volume that is covered by the reference dose and while minimizing radiation to the surrounding critical volume.

The Conformity index of radiation was defined by the Radiation Therapy Oncology Group (RTOG) as the quotient of volume covered by the reference isodose [36], which, according to ICRU, is the isodose of 95%, and the target volume designated as PTV (Planned target volume) and presented by the following equation:

$$\mathbf{CI_{RTOG} = V_{RI}/TV} \qquad \mathbf{(1)}$$

In which the V_{RI} and TV are the reference isodose volume and target volume, respectively.

The conformity index value indicates how well a treatment plan conforms to the target volume and spares the surrounding critical tissues, its values range from 0 to 1. As the ideal value of CI is one which indicates that the prescribed dose is more precisely targeted to the tumor while sparing surrounding healthy tissue with no overlap or underlap, so if its values slightly exceeds the one value, it means that some of the prescribed dose extends beyond the target volume (i.e. there is an irradiated dose in the surrounding organs), the last probability is that CI less than one value, this means part of the target volume didn't receive the full prescribed dose (i.e . less tumor control). So the closer the CI value is to one, the better the dose conformity to the PTV.

Homogeneity index (HI) [37]

HI is a quick, simple scoring tool that is used to quantify the uniformity (homogeneity) of the prescribed dose within the target volume; it also gives a general overview of the dose gradient in the target volume. It serves as quality indicator to compare different planning techniques to obtain the appropriate one [35][37-39].

As previously mentioned, that is due to the nature of the intensity-modulated techniques; the true values of maximum and minimum dose are sensitive to the dose calculation parameters and the high dose gradient, so these values are usually not reliable [36]. It is more appropriate and meaningful to use the dose to a specified fractional volume, such as the maximum and minimum dose in a volume, rather than at a point, for instance, dose to 1% or 2% and to 99% or 98% of the target volume, respectively. The Integration these reliable data leads to the HI concept that can quantitatively assess the quality of the treatment plan options. There are many formulas of HI; the most common one is [39-40]:

$$HI = (D_{2\%} - D_{98\%})/D_p \times 100 \qquad (2)$$

In which; $D_{2\%}$ meant the dose delivered to 2% of the target volume indicating the "maximum dose", $D_{98\%}$ meant the dose absorbed by 98% of the target volume, indicating the "minimum dose" and Dp is the prescribed dose of the PTV.

The ideal value of the homogeneity index is zero, which indicates that the absorbed dose distribution is almost homogeneous due to both of the maximum and minimum indicator values having the same value. If the value of HI exceeds this ideal value (0 values), homogenous dose distribution within the target volume decreases. While the homogenous dose distribution within the target volume increases when the value of HI is less than zero, according to the ICRU 83 report [41]. So the closer the HI value is to zero, the better the dose homogeneity distribution within the target volume.

3 Results and Discussion

3.1 Comparison of dosimetric parameters and results

From Figure 5 and Figure 6, which represent the isodose distribution of RA and IMRT techniques, respectively, it is very easy to conclude that RA plan gives more coverage, more conformity, and consequently more sparing for the surrounding organs than IMRT plans.

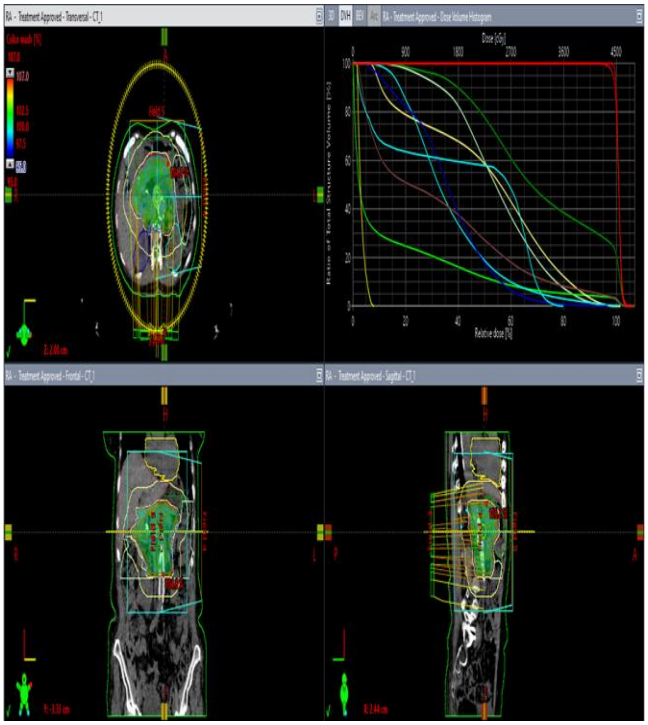


Fig. 5: RA Dose distribution for PDAC patients in the three orthogonal views and the Dose Volume Histogram.

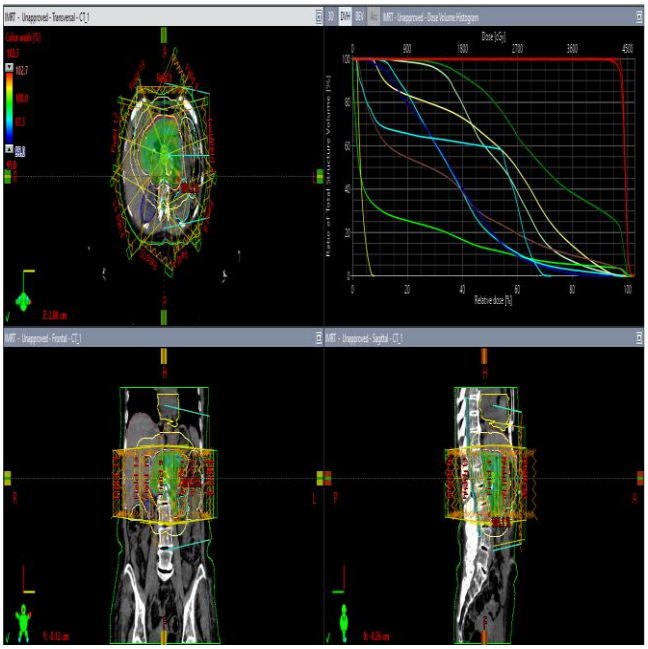


Fig. 6: IMRT Dose distribution for PDAC patients in the three orthogonal views and the Dose Volume Histogram.

From the superimposed DVHs of the two comparative strategies, the RA plan has a better dose gradient and sharpness than the IMRT plan as shown in Figure 7. However, both of them achieved the treatment plan objectives, with D95% for IMRT = 48.9 Gy and for RA = 48.6 Gy. Also, it is obvious that all organs at risk have lower dose values in the RA than those of IMRT.

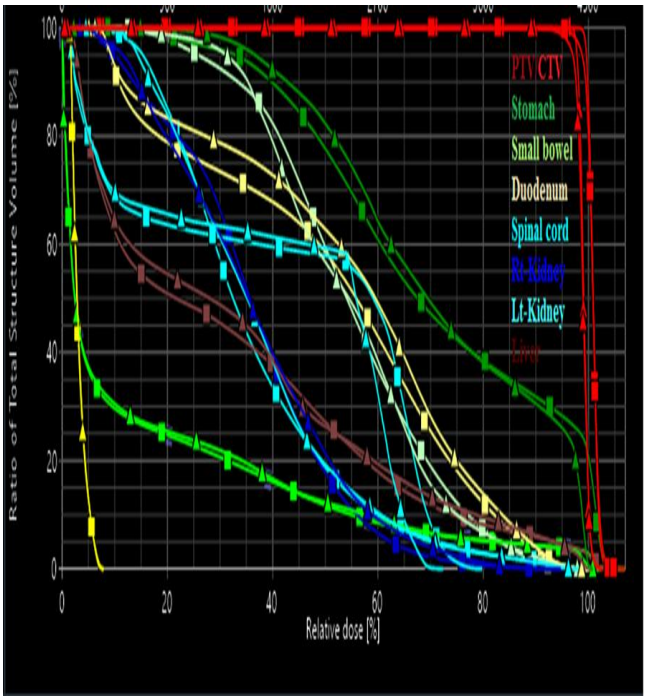


Fig.7: The Dose Volume Histogram comparison between two strategies. (▲IMRT and ■ RA).

From the DVH statistics, the conformity index data for the 30 PDAC patients can be extracted and compared; these data were displayed in Figure (8). The Figure showed that the PTV conformity index had an average value (0.84 vs. 0.9) for the IMRT and RA plans respectively. While in Figure (9), the homogeneity index data for the 30 PDAC patients can be extracted, compared and displayed. The Figure showed that the homogeneity index had an average value (0.23 vs. 0.31) for the IMRT and RA plans respectively. From the superimposed DVHs of both IMRT & VMAT strategies, it is obvious that all organs at risk have lower dose values in the RA than those of IMRT. For the main purpose of our study, we investigated the dose absorbed by both kidneys in terms of mean dose Dmean, V20 Gy, and V12 Gy. From Figure (10), the mean dose to the right kidney is Dmean (3.4-4.1) Gy vs. (8.2-9.1) Gy in RA & IMRT plans, respectively. While for the left kidney, the mean dose is in the range (4.5-5.2) Gy in RA plans vs. (9.2-10.5) Gy in the IMRT plans, which are very obvious in Figure (11).

In addition, the V20Gy of the right kidney using the VMAT technique is in the range of approximately (27.6 - 30.1) %, while by IMRT it ranges between 28.5% and 31.9 %, as shown in Figure (12). While its value in the left kidney using VMAT plans is in the range of (27 -29.6) %, and by using IMRT plans is in the range of (27.6 - 29.7) %, which is illustrated in Figure (13). It is very clear from Figure (14) that in the VMAT technique the V12Gy of the right kidney is ≤ 51.4 %, while in the IMRT technique V12Gy ≤ 50.1 %. While for the left kidney, V12Gy is ≤ (50.1 vs. 50.3) % in VMAT & IMRT plans, respectively.

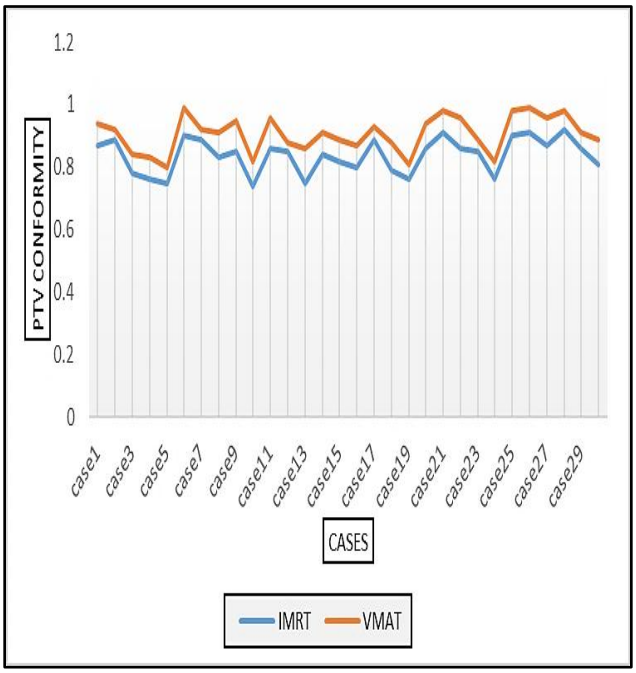


Fig. 8: The CI for the two techniques.

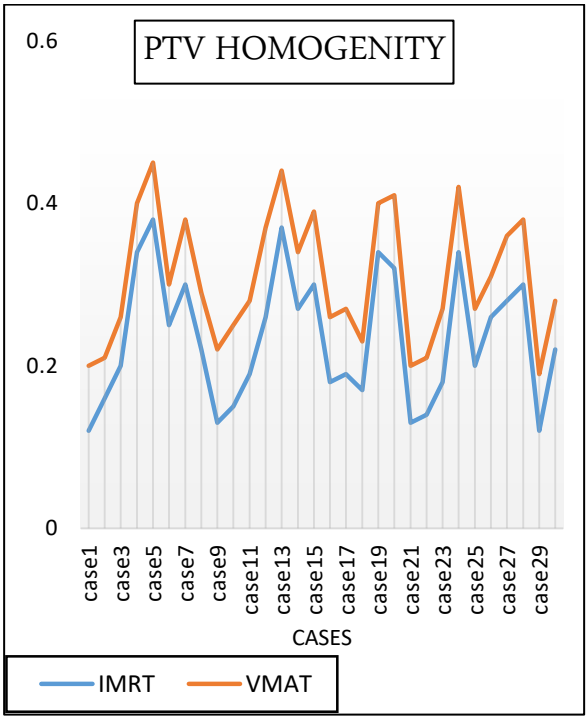


Fig. 9: The HI for the two techniques.

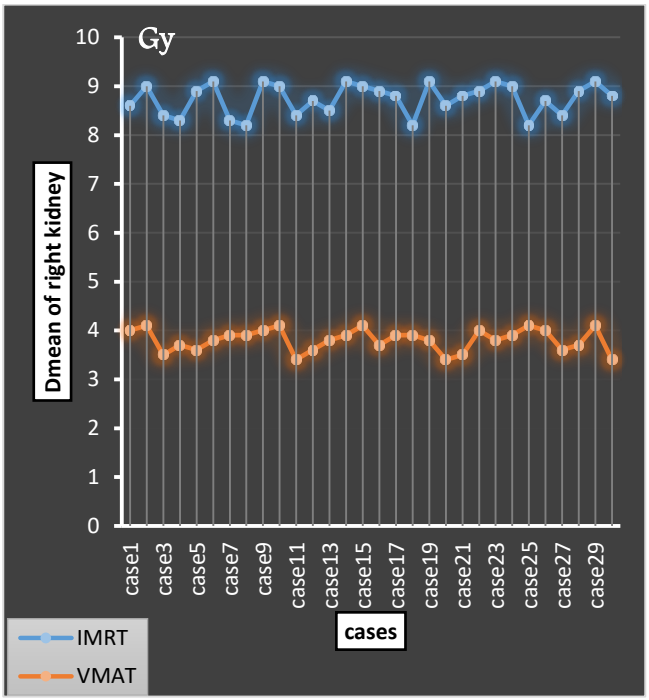


Fig. 10: D_{mean} of right kidney due to VMAT & IMRT plans.

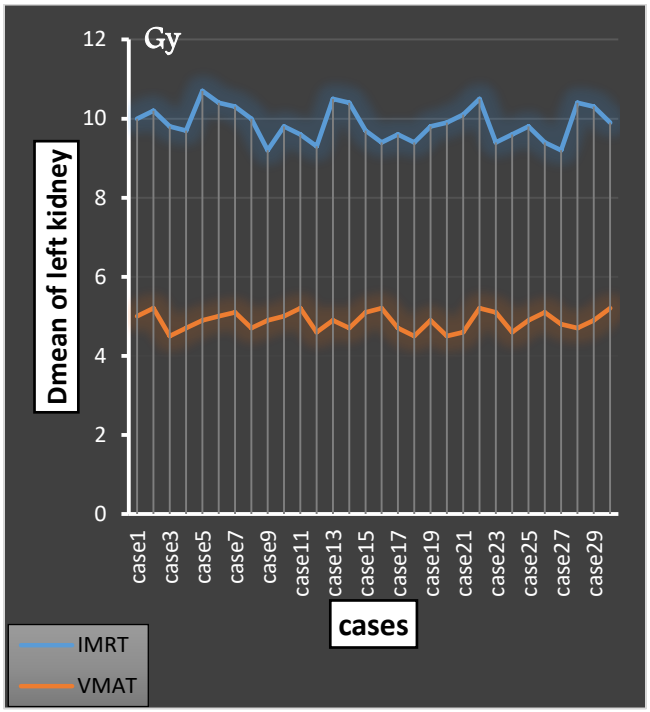


Fig. 11: D_{mean} of Left kidney due to VMAT & IMRT plans.

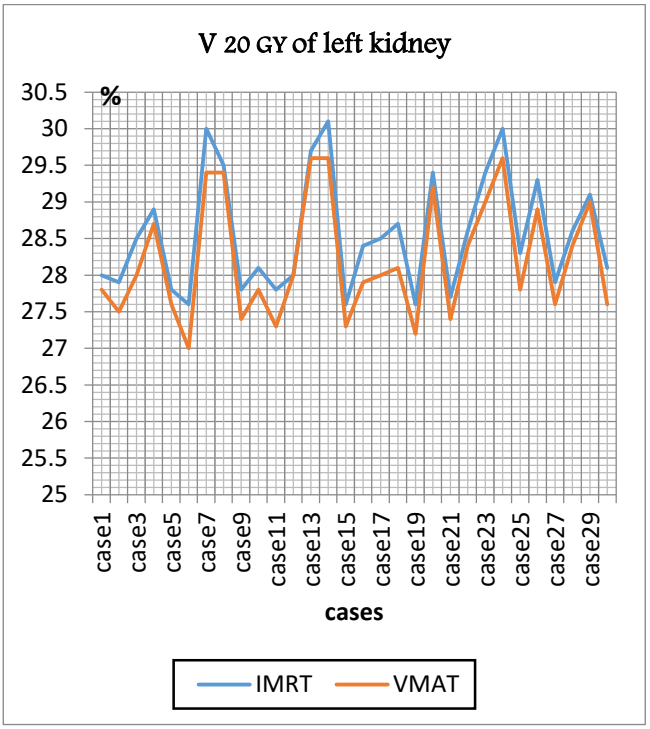


Fig.13: V12Gy of right kidney due to VMAT & IMRT plans.

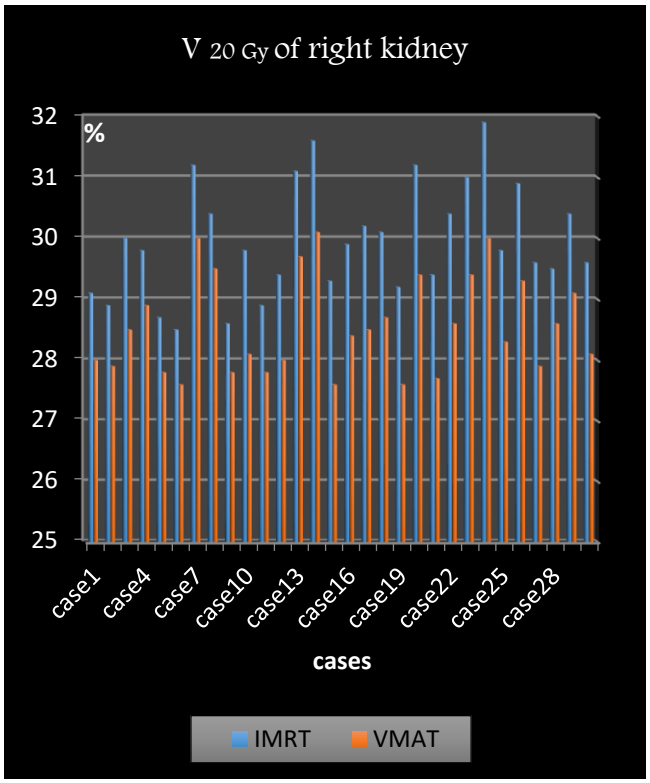


Fig. 12: V20Gy of right kidney due to VMAT & IMRT plans.

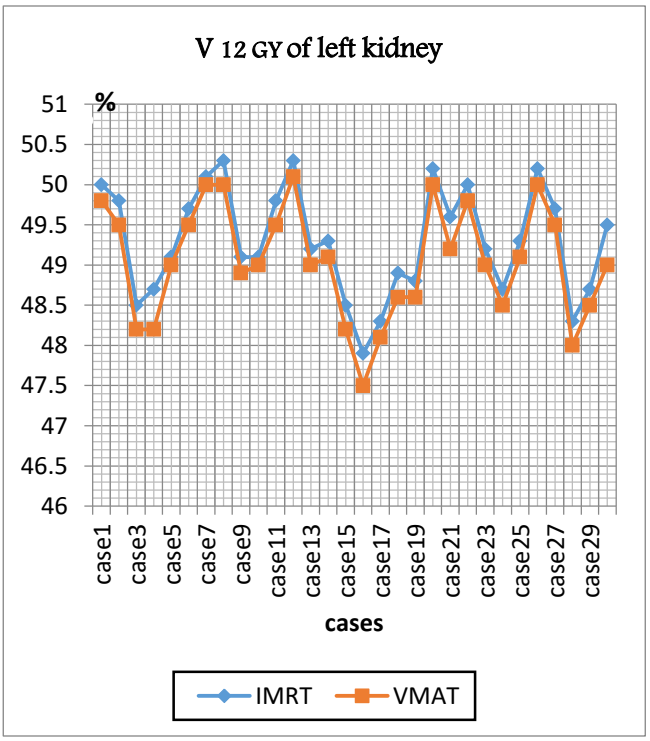


Fig.14: V12Gy of left kidney due to VMAT & IMRT plans.

3.2 Discussion

Tumor control

Although both 4D VMAT & 4D IMRT consider the tumor's movement, which allows for more accurate dose delivery was resulting in better conforming higher doses to the treatment volume and more sparing to healthy cells, 4D RA covers the target volume more than 4D IMRT in all cases despite a significant patient-to-patient variation in target volume size and shape. The best planning evaluation tools for coverage of the dose and its distribution in the target volume are CI and HI respectively. 4D RA plans have better CI values than 4D IMRT plans, which means that 4D RA gives more conformity to target volumes consequently more sparing for organs at risk that are sensitive to radiation exposure, 4D RA also produces a favorable dose gradient profile than 4D IMRT; leading 4D RA to generate better radiotherapeutic plans than 4D IMRT in PDAC patients. However, 4D IMRT provided more dose homogeneity than 4D RA, regardless this constraint may be unnecessarily confining if the main goal is to achieve OAR sparing rather than target dose homogeneity.

Bilateral kidney survival

From the resultant value of the mean dose of both kidneys, it was very clear that the 4D RA plans have a significant reduction in the mean dose to both kidneys compared to the 4D IMRT plans, which was statistically proven that 4D RA is superior in bilateral kidney preservation from renal failure compared to 4D IMRT in patients with PDAC. Although for the left kidney, it was found that the V20Gy and V12Gy values were slightly different between the two comparative techniques, 4D RA and 4D IMRT plans, and appeared to be statistically overlapping. While for the right kidney, the V20Gy values have greater percentage by the 4D IMRT than the 4D VMAT technique, but the V12Gy values have greater percentage by the 4D VMAT than the 4D IMRT technique. This means that at high dose values, the percentage of right kidney volume that absorbed the irradiated dose is more in the 4D IMRT than the 4D VMAT technique. On the contrary, at low dose values, the percentage of right kidney volume that absorbed irradiated dose is more in the 4D VMAT than the 4D IMRT technique, although both of them are under the tolerance dose **[**45-49**]**.

As the kidney is classified as a parallel organ, the radiation-associated injury is more sensitive to the average dose over the whole organ volume, so the most common tolerance dose used for planning technique evaluation is Dmean, which is significantly reduced in RA plans. Therefore, 4D RA provides more protective effect for bilateral kidneys that can achieve an ongoing goal for sparing bilateral kidneys during radiotherapy for pancreatic malignancies compared to 4D IMRT; this result is consistent with many previous dosimetric studies as SEZEN, et al. study, Ali, et al. study, and Hegazy MW, et al. study **[**42-44**]**.

4 Conclusions

As 4D VMAT demonstrates strong potential for reducing bilateral kidney toxicity, it is more dramatic in protecting them from the probability of chronic kidney diseases and renal failure. This advantage suggests that the prescribed dose could be safely escalated and more effectively delivered to the target volume, thereby improving tumor control while reducing complication rates. For pancreatic cancer, pancreatic motion is an essential problem and represents a major challenge for precise radiation delivery; however, by using the Real-Time Tumor-Tracking (RTRT) technology, the margins of moving target volume and the possible errors in target localization were reduced. The RTRT enables the RA to reduce the uncertainty of moving tumors by offering shorter overall treatment time compared to 4D IMRT as well as it also offers a favorable dose gradient profile, superior conformity, enhanced normal tissue sparing, particularly of the kidneys, faster treatment delivery, and reduced monitor units (MUs). Although the present study included a relatively small sample size, the results indicate multiple advantages of combining real-time tumor tracking with the VMAT technique. Further comparative studies between modulated radiotherapy techniques with and without real-time tumor-tracking are required to confirm our study results.

Despite the small sample size, the results are encouraging and strongly suggested that RA-RTRT could serve as a standard treatment option for PDAC. Further large-scale studies and clinical trials are needed to validate its long-term efficacy and safety.

Although limited by a small sample size, the findings are encouraging and strongly suggest that RA-RTRT could serve as a standard treatment option for PDAC. Further large-scale studies and clinical trials are needed to validate its long-term efficacy and safety.

Acknowledgement

Our utmost gratitude and thanks to **Prof. Dr. Mostafa El sayed Abd El wanis** , Professor of Radiotherapy South Egypt Cancer Institute, Assuit University, for his supervising, grateful help, encouragement , stimulating discussion, reading , criticizing the manuscript and guidance assistance to carry out this work.

References

[1] Mizrahi, Jonathan D., Rishi Surana, Juan W. Valle, and Rachna T. Shroff. "Pancreatic cancer." The Lancet 395(10242), 2008-2020, 2020.

Pishvaian, Michael J., and Jonathan R. Brody. "Therapeutic Implications of Molecular Subtyping for Pancreatic Cancer." Oncology (Williston Park, NY) 31(3), 159-66 , 2017.

[2] Everett, Jessica N., Diane M. Simeone, Eric J. Duell, Donghui Li, and Núria Malats. "Pancreatic cancer." In World Cancer Report: Cancer research for cancer prevention. International Agency for Research on Cancer, 2020.

[3] Von Hoff, Daniel D., Douglas Brian Evans, and Ralph H. Hruban, eds. Pancreatic cancer. Jones & Bartlett Learning, 2005.

[4] Taylor, Alexandra, and M. E. B. Powell. "Intensity-modulated radiotherapy—what is it?." Cancer Imaging 4(2), 68, 2004.

[5] Purdy, J. A. Intensity-modulated radiation therapy. International Journal of Radiation Oncology* Biology* Physics, 35(4), 845-846, 1996.

[6] Webb, S. The physical basis of IMRT and inverse planning. The British journal of radiology, 76(910), 678-689, 2003.

[7] Small, W. Perez and Brady's Principles and Practice of Radiation Oncology. JAMA, 301(19), 2046-2051, 2009.

[8] Teoh, M., Clark, C. H., Wood, K., Whitaker, S., & Nisbet, A. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. The British journal of radiology, 84(1007), 967-996, 2011.

[9] Nakamura, Katsumasa, Tomonari Sasaki, Saiji Ohga, Tadamasa Yoshitake, Kotaro Terashima, Kaori Asai, Keiji Matsumoto, Yoshiyuki Shioyama, and Hiroshi Honda. "Recent advances in radiation oncology: intensity-modulated radiotherapy, a clinical perspective." International journal of clinical oncology 19(4), 564-569, 2014.

[10] Bortfeld, Thomas, Kimmo Jokivarsi, Michael Goitein, Jong Kung, and Steve B. Jiang. "Effects of intra-fraction motion on IMRT dose delivery: statistical analysis and simulation." Physics in Medicine & Biology 47(13), 2203, 2002.

[11] Sawant, Amit, Raghu Venkat, Vikram Srivastava, David Carlson, Sergey Povzner, Herb Cattell, and Paul Keall. "Management of three-dimensional intrafraction motion through real-time DMLC tracking." Medical physics 35(5), 2050-2061, 2008.

[12] Sawant, Amit, Ryan L. Smith, Raghu B. Venkat, Lakshmi Santanam, Byungchul Cho, Per Poulsen, Herbert [13] Cattell, Laurence J. Newell, Parag Parikh, and Paul J. Keall. "Toward submillimeter accuracy in the management of intrafraction motion: the integration of real-time internal position monitoring and multileaf collimator target tracking." International Journal of Radiation Oncology* Biology* Physics 74(2), 575-582, 2009.

[14] Fakhrian, K., M. Oechsner, S. Kampfer, T. Schuster, M. Molls, and H. Geinitz. "Advanced techniques in neoadjuvant radiotherapy allow dose escalation without increased dose to the organs at risk: planning study in esophageal carcinoma." 293-300, 2013.

[15] Sapkaroski, D., Osborne, C., & Knight, K. A. A review of stereotactic body radiotherapy–is volumetric modulated arc therapy the answer? Journal of Medical Radiation Sciences, 62(2), 142-151, 2015.

[16] Teoh, M., Beveridge, S., Wood, K., Whitaker, S., Adams, E., Rickard, D., ... & Clark, C. H. Volumetric-modulated arc therapy (RapidArc) vs. conventional fixed-field intensity-modulated radiotherapy for 18F-FDG-PET-guided dose escalation in oropharyngeal cancer: A planning study. Medical Dosimetry, 38(1), 18-24,2013.

[17] Teoh, M., Clark, C. H., Wood, K., Whitaker, S., & Nisbet, A. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. The British journal of radiology, 84(1007), 967-996,2011.

[18] Popple, R. A., & Balter, P. A. 2.10. Because of the advantages of rotational techniques, conventional IMRT will soon become obsolete. Controversies in Medical Physics: a Compendium of Point/Counterpoint Debates Volume 3, 150, 2017.

[19] Ong, C. L., Verbakel, W. F., Cuijpers, J. P., Slotman, B. J., Lagerwaard, F. J., & Senan, S. Stereotactic radiotherapy for peripheral lung tumors: a comparison of volumetric modulated arc therapy with 3 other delivery techniques. Radiotherapy and oncology, 97(3), 437-442, 2010.

[20] Palma, D. A., Verbakel, W. F., Otto, K., & Senan, S. New developments in arc radiation therapy: a review. Cancer treatment reviews, 36(5), 393-399, 2010.

[21] Verbakel, W. F., Cuijpers, J. P., Hoffmans, D., Bieker, M., Slotman, B. J., & Senan, S. Volumetric intensity-modulated arc therapy vs. conventional IMRT in head-and-neck cancer: a comparative planning and dosimetric study. International Journal of Radiation Oncology* Biology* Physics, 74(1), 252-259, 2009.

[22] Shintani, Takashi, Mitsuhiro Nakamura, Yukinori Matsuo, Yuki Miyabe, Nobutaka Mukumoto, Takamasa Mitsuyoshi, Yusuke Iizuka, and Takashi Mizowaki. "Investigation of 4D dose in volumetric modulated arc therapy-based stereotactic body radiation therapy: does fractional dose or number of arcs matter?." Journal of Radiation Research 61(2), 325-334, 2020.

[23] Grégoire, Vincent, and Thomas R. Mackie. "State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83)." Cancer/radiothérapie 15(6-7), 555-559, 2011.

[24] Yan, Yue, Poonam Yadav, Michael Bassetti, Kaifang Du, Daniel Saenz, Paul Harari, and Bhudatt R. Paliwal. "Dosimetric differences in flattened and flattening filter-free beam treatment plans." Journal of Medical Physics 41(2), 92-99, 2016.

[25] Marks, Lawrence B., Ellen D. Yorke, Andrew Jackson, Randall K. Ten Haken, Louis S. Constine, Avraham Eisbruch, Søren M. Bentzen, Jiho Nam, and Joseph O. Deasy. "Use of normal tissue complication probability models in the clinic." International Journal of Radiation Oncology* Biology* Physics 76(3), S10-S19, 2010.

[26] Shirato, Hiroki, Shinichi Shimizu, Tatsuya Kunieda, Kei Kitamura, Marcel Van Herk, Kenji Kagei, Takeshi Nishioka et al. "Physical aspects of a real-time tumor-tracking system for gated radiotherapy." International Journal of Radiation Oncology* Biology* Physics 48(4), 1187-1195, 2000.

[27] D D'Souza, Warren, Shahid A. Naqvi, and X. Yu Cedric. "Real-time intra-fraction-motion tracking using the treatment couch: a feasibility study." Physics in Medicine & Biology 50(17), 4021, 2005.

[28] Paik, E. K., Kim, M. S., Choi, C. W., Jang, W. I., Lee, S. H., Choi, S. H., ... & Lee, D. H. Dosimetric comparison of volumetric modulated arc therapy with robotic stereotactic radiation therapy in hepatocellular carcinoma. Radiation Oncology Journal, 33(3), 233, 2015.

[29] Jones, Douglas. "ICRU report 50—prescribing, recording and reporting photon beam therapy." 833-834, 1994.

[30] Levitt, Seymour H., James A. Purdy, Carlos A. Perez, and Srinivasan Vijayakumar. Technical basis of radiation therapy. New York, NY: Springer, 2012.

[31] Stroom, Joep C., and Ben JM Heijmen. "Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report." Radiotherapy and oncology 64(1), 75-83, 2002.

[32] Small, William. "Perez and Brady's principles and practice of radiation oncology." JAMA 30(19), 2046-2051, 2009.

[33] Goitein, Michael. "The comparison of treatment plans." In Seminars in Radiation Oncology, vol. 2(4), 246-256,WB Saunders, 1992.

[34] Al-Rawi, Salam Abdulrazzaq Ibrahim, Hassan Abouelenein, Magdy Mohammed Khalil, Haidar Hamza Alabdei, Awf Abdulrahman Sulaiman, Dalya Saad Al-Nuaimi, and Mohamed El-Sayed EL Nagdy. "Evaluation of conformity and homogeneity indices consistency throughout the course of head and neck cancer treatment with and without using adaptive volumetric modulated arc radiation therapy." Advances in radiation oncology 7(5), 100905, 2022.

[35] Feuvret, Loïc, Georges Noël, Jean-Jacques Mazeron, and Pierre Bey. "Conformity index: a review." International Journal of Radiation Oncology* Biology* Physics 64(2), 333-342, 2006.

[36] Shaw, Edward, Robert Kline, Michael Gillin, Luis Souhami, Alan Hirschfeld, Robert Dinapoli, and Linda Martin. "Radiation Therapy Oncology Group: radiosurgery quality assurance guidelines." International Journal of Radiation Oncology* Biology* Physics 27(5), 1231-1239,1993.

[37] Helal, Azza, and Abbas Omar. "Homogeneity index: effective tool for evaluation of 3DCRT." Pan Arab J Oncol 8(2), 20-23, 2015.

[38] Gong, Youling, Jin Wang, Sen Bai, Xiaoqin Jiang, and Feng Xu. "Conventionally-fractionated image-guided intensity modulated radiotherapy (IG-IMRT): a safe and effective treatment for cancer spinal metastasis." Radiation oncology 3(1), 11, 2008.

[39] Wu, Qiuwen, Radhe Mohan, Monica Morris, Andrew Lauve, and Rupert Schmidt-Ullrich. "Simultaneous integrated boost intensity-modulated radiotherapy for locally advanced head-and-neck squamous cell carcinomas. I: dosimetric results." International Journal of Radiation Oncology* Biology* Physics 56(2), 573-585, 2003.

[40] Yoon, Myonggeun, Sung Yong Park, Dongho Shin, Se Byeong Lee, Hong Ryull Pyo, Dae Yong Kim, and Kwan Ho Cho. "A new homogeneity index based on statistical analysis of the dose–volume histogram." Journal of applied clinical medical physics 8(2), 9-17, 2007.

[41] Hodapp, N. "The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT)." Strahlentherapie und Onkologie: Organ der Deutschen Rontgengesellschaft...[et al] 188(1), 97-99, 2012.

Bölükbaşi, Yasemin, Yücel Sağlam, Duygu Sezen, Z. Vildan Alpan, Steve Kirsner, and Uğur Selek. "Volumetric [42] Arc Therapy Seems More Promising for Sparing Organs at Risk in Adjuvant Postoperative Radiotherapy for Pancreatic Adenocarcinoma than Step-and-Shoot Intensity-Modulated Radiotherapy." Turkish Journal of Oncology 32(2) , 2017.

[43] Ali, Arif N., Anees H. Dhabaan, Christie S. Jarrio, Arsalan K. Siddiqi, and Jerome C. Landry. "Dosimetric comparison of volumetric modulated arc therapy and intensity-modulated radiation therapy for pancreatic malignancies." Medical Dosimetry 37(3), 271-275, 2012.

[44] Hegazy MW, Soliman MI, Khalil NS, Mahmoud A, Amgad S, et al. (2023) Intensity Modulated Radiation Therapy vs. Volumetric Modulated Arc Therapy in Locally Advanced Unresectable Pancreatic Cancer: Dosimetric Study. Int J Cancer Clin Res 10:183. doi.org/10.23937/2378-3419/1410183.

[45] Saleh Alashrah, Sivamany Kandaiya, Nabil Maalej, A. El-Taher., (2014).Skin Dose Measurements Using Radiochromic Films, TLDs, and Ionization Chamber and Comparison with Monte Carlo Simulation. Journal of Radiation Protection Dosimetry, (162) 338-344.

[46] Alsayyari, MAA Omer, Atef El-Taher., (2018). Assessment of Exposure Dose Due to Radioactive Sources at Lab of Radiology Department-Qassim University. Journal of Medical Sciences. 18 (2), 103-107.

[47] Gena Mohamed, KM El-Shahat, M Salem, Atef El-Taher., (2021). Use of Amorphous Silicon (ASi) Electronic Portal Imaging Devices for Other applications for Linear Accelerator Quality Assurance, Iranian Journal of Medical Physics 18 (4), 285-29.

[48] Gena M.A.H , Khalid. M .El-Shahat , , M.Y. Salem and Ahmed Ali , Atef El-Taher ., (2023). The Influence of Electronic Portal Imaging Devices (EPIDs) used in Radiotherapy: Image Quality and Dose Measurements. J. Rad. Nucl. Appl. 8, No. 3, 237-243.

[49] Saleh Alashrah and A. El-Taher., (2015). Intensity-modulated radiation therapy plans verification using a Gaussian convolution kernel to correct the single chamber response function of the I'mRT MatriXX array. Journal of Applied Science, 15(3) 483-491.