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Ipsilateral kidney sparing in treatment of pancreatic malignancies using volumetric-modulated arc therapy avoidance sectors

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ABSTRACT

Recent research has shown treating pancreatic cancer with volumetric-modulated arc therapy (VMAT) to be superior to either intensity-modulated radiation therapy or 3-dimensional conformal radiotherapy (3D-CRT), with respect to reducing normal tissue toxicity, monitor units, and treatment time. Furthermore, using avoidance sectors with RapidArc planning can further reduce normal tissue dose while maintaining target conformity. This study looks at the methods in reducing dose to the ipsilateral kidney, in pancreatic head cases, while observing dose received by other critical organs using avoidance sectors. Overall, 10 patients were retrospectively analyzed. Each patient had preoperative/unresectable pancreatic tumor and were selected based on the location of the right kidney being situated within the traditional 3D-CRT treatment field. The target planning target volume ($286.97 \pm 85.17\ cm^3$) was prescribed to 50.4 Gy using avoidance sectors of 30°, 40°, and 50° and then compared with VMAT as well as 3D-CRT. Analysis of the data shows that the mean dose to the right kidney was reduced by 11.6%, 15.5%, and 21.9% for avoidance angles of 30°, 40°, and 50°, respectively, over VMAT. The mean dose to the total kidney also decreased by 6.5%, 8.5%, and 11.0% for the same increasing angles. Spinal cord maximum dose, however, increased as a function of angle by 3.7%, 4.8%, and 6.1% compared with VMAT. Employing avoidance sector angles as a complement to VMAT planning can significantly reduce high dose to the ipsilateral kidney while not greatly overdosing other critical organs.

Introduction

Surgery serves as the only potentially curative treatment for pancreatic cancer. Unfortunately, resectable tumors account for only about 20% of all cases.[1,2] The remaining 80% of the cases are left unresected, with radiation therapy with concurrent chemotherapy as the definitive treatment. This is because of the tumor being considered unresectable from either blood vessel encasement or distant metastasis.

Pancreatic tumor is often treated with the traditional 4-field box technique using 3-dimensional conformal radiotherapy (3D-CRT) where the use of multileaf collimators (MLCs) shape each field to conform to the tumor. However, the location of the tumor is situated in the upper abdomen and surrounded by a number of critical organs such as the liver, stomach, spinal cord, kidneys, and small bowel, which are all exposed to radiation. Oblique angles have been employed with the aim of avoiding one of these organs, which generally tends to be either kidney.

Intensity-modulated radiotherapy (IMRT) uses an arrangement of MLC positions to deliver beam fluence, which enables better dose conformity to the target compared with 3D-CRT. The conformity index is a measure of how well a referenced prescription dose volume fits to the target volume. Because of improved conformity, nearby organs are able to be better spared due to the tighter high-dose cloud. Zhen *et al.*[3] have demonstrated IMRT to be superior with better conformal dose distribution, reduced dose to nearby tissue, and possible dose escalation. Further studies have also shown better conformity[4] and reduced dose to the liver, stomach, and bowel.[5,6] Because of an improved conformity index, where higher isodose lines better fit to the shape of the target and pull undesirable dose from nearby organs at risk, acute gastrointestinal (grades 3 and 4) toxicities were minimized.[7]

Arc or rotational therapy allows the gantry to continuously rotate around the patient, with the beam on, as the dynamic MLC leaves modulate the beam. This technique allows a more conformal fit to the target with high-dose regions compared with the fixed-beam technique of IMRT.[8] In addition to better conformity,

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VMAT was proven to have lesser monitor units and shorter treatment time.[9,10] Organs, *e.g.*, liver, small bowel, spinal cord, and bilateral kidneys, were also shown to have similar or better dosimetric results with VMAT over IMRT, as well as 3D-CRT.[11]

Because VMAT delivers radiation beams continuously in a complete gantry rotation, patients are exposed to low dose spillage in a large region outside of the intended target. The corollary is that the high dose spillage can be more readily confined to a desired region. This is particularly useful if we need to reduce high dose to an area close to the planning target volume (PTV). For kidneys that are peripheral and away from the tumor, 3D-CRT fields can be angled in a way to avoid either or both kidneys (Fig. 1A). However, for kidneys that are in the treatment field, high dose to the ipsilateral kidney cannot be avoided with any 4-field configuration (Fig. 1B). This study looks at using VMAT to treat tumors located at the pancreatic head, specifically when the right kidney is located within the target's treatment field. To further reduce high dose to the ipsilateral kidney, several avoidance sector angles were used during arc therapy treatment.

The ipsilateral kidney is subjected to high doses as a result of its proximity to the tumor. Therefore, the use of avoidance sectors can be justified in some cases. There are instances when a patient may have renal dysplasia and the ipsilateral kidney is the only one functioning of the two. Another instance being if the ipsilateral kidney is the sole kidney because of renal agenesis or nephrectomy. In these cases, sparing the right kidney is necessary.

Renal toxicity is a late-responding complication where injury due to radiation occurs within several months to years. Clinical end points of renal toxicity include, but are not limited to, malignant hypertension, edema, and dyspnea.[12] Patient data from studies have been sparse owing to the latent period of the late chronic effects of radiation-induced renal injury.

VMAT has been shown to have superior dosimetric results in terms of organ sparing and target conformity compared with 3D-CRT. In the section Discussion, the 3D-CRT plan comparison is omitted to focus on the results of planning with VMAT using avoidance sectors.

Methods and Materials

Patient selection and simulation

Overall, 10 patients diagnosed with malignancies to the pancreatic head, without previous resection, were retrospectively selected for this study. Furthermore, each case had the ipsilateral kidney located within the treatment field of the target. All patients, positioned supine with arms up and immobilized, underwent computed tomography simulation with a GE LightSpeed scanner (GE Medical Systems, Milwaukee, WI). Each resulting image set had 2.5-mm image slice thickness, which is then transferred to the Eclipse Treatment Planning System 10.0 (Varian Medical Services, Palo Alto, CA) for contouring and planning.

Target and critical organs

The gross target volume (GTV) was the visible preoperative tumor delineated by the physician. The motion of the pancreas has been shown to preferentially move during respiration 1.5 to 2.0 cm in superior-inferior direction and 0.5 to 1.0 cm radially.[13,14] Respiratory-gating treatment is a technique where the beam is delivered to the tumor at a particular respiratory phase. The advantage of this technique is that the planning margins can be smaller so less normal tissue is irradiated. However, because the beam is on at certain phases, treatment time is significantly increased. This may lead to patient discomfort and restlessness, which may cause adverse results if the target is shifted outside of the treatment field. The PTV for this study included a 2.0- to 2.5-cm superior-inferior expansion and a 1.5- to 2.0-cm radial expansion off the GTV. Gated treatment was not used in this study, and the margins for the PTV account for respiratory movement of the GTV. An additional 1-mm expansion off the PTV was created to allow greater coverage during VMAT optimization. The critical organs at risk were both right and left kidneys, small bowel, liver, and spinal cord. The small bowel was contoured as individual loops. Additionally, the planning risk volume was created as a 1-mm expansion from the necessary critical organs that overlapped with the PTV. The planning risk volume structures were then cropped from the PTV by 3 mm and were used as secondary structures for optimization. Couch structures, particular to a linear accelerator, were included to account for beam attenuation.

Treatment planning

The PTV target, for all 10 patients, had a mean volume of 286.97 ± 85.17 cm^3 and was treated with a prescription dose of 50.4 Gy in 28 fractions (1.8 Gy/fx). Each plan ensured that 100% of the PTV was receiving at least 95% of the prescription dose. 3D-CRT technique consisted of a 4-field arrangement of 23-MV photon beams. Fields were set up using either a 4-field box arrangement or, when necessary, oblique angles to avoid the ipsilateral kidney as much as possible. Appropriate wedging and beam weighting were used to achieve optimal target coverage. The VMAT (RapidArc) technique used 6-MV photon beams with 2 full arcs, clockwise (start angle: 181.0°; stop angle: 179.0°) and counterclockwise (start angle: 179.0°; stop angle: 181.0°), and the isocenter set to the center of the PTV. Settings for RapidArc included a 30° collimator rotation, 600 MU/min dose rate, 2.5-mm calculation grid size, and air cavity and heterogeneity corrections enabled. Calculations were computed using the Anisotropic Analytical Algorithm 10.0.28.

In addition to the RapidArc technique, avoidance sectors were used to further spare the ipsilateral kidney. Defining avoidance sectors during VMAT optimization allow the gantry to rotate with the beam off at preset angles. For this study, to avoid high dose to the right kidney, the beam is turned off (zero monitor unit output) when the beam path is obstructed by the critical organ. Angles were set by bisecting the right kidney with respect to the isocenter, and sector angles were chosen such that the beam had no output for 30° (VMAT_30), 40° (VMAT_40), and 50° (VMAT_50) of the total arc rotation.

Results

In total, 5 different treatment techniques were used, and each plan had at least 95% dose coverage to 100% of the PTV. Results from 3D-CRT, VMAT, and VMAT with different avoidance sectors (30°, 40°, and 50°) are presented in Tables 1 and 2. Each parameter was averaged over all 10 patients, and the range included the minimum and the maximum value. As expected, increasing avoidance angles preferentially to the ipsilateral kidney will cause better sparing. This results in other critical organs to share the migrated dose.

Comparisons between VMAT and VMAT_##, where ## denotes sector angle, were performed using a paired, 2-tailed Student t-test. A $p \leq 0.05$ indicates that there is a statistical significance between the VMAT technique and the avoidance angle. However, a $p > 0.05$ denotes no statistical significance between the 2 treatment techniques

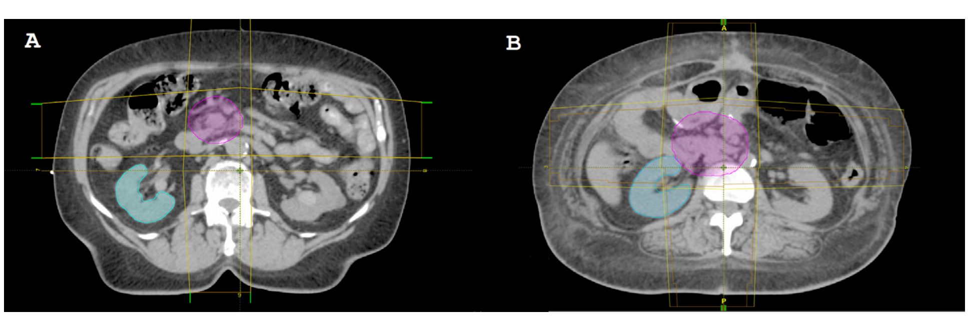

Fig. 1. Axial scan of ipsilateral kidney (A) peripheral and (B) proximal to the PTV.