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Volumetric-modulated arc radiotherapy for pancreatic malignancies: Dosimetric comparison with sliding-window intensity-modulated radiotherapy and 3-dimensional conformal radiotherapy

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ABSTRACT

Volumetric-modulated arc radiotherapy (VMAT) is an iteration of intensity-modulated radiotherapy (IMRT), both of which deliver highly conformal dose distributions. Studies have shown the superiority of VMAT and IMRT in comparison with 3-dimensional conformal radiotherapy (3D-CRT) in planning target volume (PTV) coverage and organs-at-risk (OARs) sparing. This is the first study examining the benefits of VMAT in pancreatic cancer for doses more than 55.8 Gy. A planning study comparing 3D-CRT, IMRT, and VMAT was performed in 20 patients with pancreatic cancer. Treatments were planned for a 25-fraction delivery of 45 Gy to a large field followed by a reduced-volume 8-fraction external beam boost to 59.4 Gy in total. OARs and PTV doses, conformality index (CI) deviations from 1.0, monitor units (MUs) delivered, and isodose volumes were compared. IMRT and VMAT CI deviations from 1.0 for the large-field and the boost plans were equivalent (large field: 0.032 and 0.046, respectively; boost: 0.042 and 0.037, respectively; $p > 0.05$ for all comparisons). Both IMRT and VMAT CI deviations from 1.0 were statistically superior to 3D-CRT (large field: 0.217, boost: 0.177; $p < 0.05$ for all comparisons). VMAT showed reduction of the mean dose to the boost PTV (VMAT: 61.4 Gy, IMRT: 62.4 Gy, and 3D-CRT: 62.3 Gy; $p < 0.05$). The mean number of MUs per fraction was significantly lower for VMAT for both the large-field and the boost plans. VMAT delivery time was less than 3 minutes compared with 8 minutes for IMRT. Although no statistically significant dose reduction to the OARs was identified when comparing VMAT with IMRT, VMAT showed a reduction in the volumes of the 100% isodose line for the large-field plans. Dose escalation to 59.4 Gy in pancreatic cancer is dosimetrically feasible with shorter treatment times, fewer MUs delivered, and comparable CIs for VMAT when compared with IMRT.

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Introduction

Pancreatic cancer continues to be a serious cause of morbidity and mortality worldwide.[1] The treatment of pancreatic cancer commonly consists of a trimodality approach of chemotherapy, radiation therapy, and surgical resection. Owing to the location of the tumor close to critical normal tissues, toxicity is a common occurrence. Traditionally, 3-dimensional conformal radiation therapy (3D-CRT) consisting of a 4-field radiation technique has been used for pancreatic malignancies. In randomized studies, the Radiation Therapy Oncologic Group grades 3 to 4 nausea or vomiting and diarrhea has been shown to affect 11% and 17% of patients treated with 3D-CRT, respectively.[2]

To further improve the dose conformality and decrease the toxicity seen with 3D-CRT, intensity-modulated radiation therapy (IMRT) has been increasingly used to treat pancreatic malignancies. Dosimetric analyses comparing IMRT with 3D-CRT have shown an improved ability of IMRT to achieve normal tissue dose goals.[3,4] Additionally, it has been shown that nausea, vomiting, and diarrhea are markedly reduced in IMRT as compared with 3D-CRT, with very few patients experiencing Radiation Therapy Oncologic Group grades 3 to 4 nausea or vomiting.[5] However, given the increased number of beams used for treatment as compared with

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3D-CRT, IMRT is associated with longer treatment times, negatively affecting patient comfort and intrafraction patient motion.

Volumetric-modulated arc therapy (VMAT) is a further iteration of IMRT, in which the radiation dose is delivered through 1 or more dynamically modulated arcs, allowing for a more rapid and highly conformal radiation treatment while delivering fewer monitor units (MUs).[6] Dosimetric comparisons of VMAT as compared with IMRT and 3D-CRT have recently been shown for many disease sites: the head and neck,[7,8] prostate,[9] brain,[10] anus,[11] and cervix.[12,13] To date, there have been only 2 dosimetric analyses of VMAT in patients with pancreatic cancer,[14,15] with prescribed doses ranging from 48.7 to 55.8 Gy.

There are currently no dosimetric analyses in peer-reviewed journals examining various radiation treatment techniques in patients with pancreatic cancer with prescribed doses more than 55.8 Gy. In this study, we dosimetrically compared 3D-CRT, IMRT, and VMAT with prescribed doses of 59.4 Gy in 20 patients with pancreatic cancer who did and did not undergo previous resection. Additionally, the ability of VMAT to meet normal tissue tolerances despite the dose escalation to 59.4 Gy was evaluated.

Methods and Materials

Patients

A retrospective planning study was performed in 20 patients with advanced pancreatic cancer who had undergone a pancreaticoduodenectomy or whose tumors were unresectable. Data collection was approved by the institutional review board.

Patient immobilization was achieved using the BodyFIX whole-body double-vacuum immobilization system (Medical Intelligence, Schwabmuenchen, Germany) without diaphragmatic control and with abdominal compression.[16] Each patient underwent a free-breathing respiratory-correlated 4D computed tomography (4D CT) on a dedicated 16-slice helical big-bore simulator (Philips Medical Systems, Cleveland, OH) in the supine position.

Treatment planning

The 4D CT scans were reconstructed in 10 equally spaced time bins of 3-mm slice thickness using respiratory phase binning. The 4D maximum-intensity projection image data set, the free-breathing CT, and the average-intensity projection CT were all exported to a treatment planning platform (Eclipse, Varian Medical Systems, Palo Alto, CA) for target and organs-at-risk (OARs) segmentation. For the large-field plans, an internal target volume based on the maximum-intensity projection, the free-breathing CT, and the 10 respiratory phases of the 4D CT was created. For postoperative patients, the large-field contours included the postoperative bed and the at-risk nodal regions (celiac, superior mesenteric artery, periaortic, porta hepatis, or peripancreatic). For nonoperative patients, the large-field contours included the pancreas and the at-risk nodal volumes mentioned previously. The planning target volume (PTV) was obtained by uniformly expanding the internal target volume with a 5-mm margin. Depending on the tumor location, OARs such as the spinal cord, kidneys, liver, and stomach were contoured on the average-intensity projection CT data set. The average-intensity projection CT was also used for dose calculation. Individual isodose constraints were placed to ensure that the maximal tolerated doses to the OARs per published Quantitative Analysis of Normal Tissue Effects in the Clinic guidelines were not exceeded.[17] The summated large-field and boost constraints used during planning included the following: the spinal cord $D_{max} < 40$ Gy; the left or the right kidney $D_{20\%} < 20$ Gy, $D_{10\%} < 26$ Gy; and the liver $D_{30\%} < 25$ Gy. All plans were computed such that the prescribed dose encompassed at least 95% of the PTV. In addition to the primary course of treatment of 45 Gy, a boost plan (encompassing the gross tumor for nonoperative patients or the postoperative bed for postoperative patients) was created on a new planning CT data set with a resultant cumulative dose of 59.4 Gy (1.8 Gy/fraction).

Planning techniques

The imaging data were electronically transferred to the Eclipse radiation therapy planning system. A total of 3 different planning techniques were compared in the study: 3D-CRT, IMRT, and VMAT. All plans were created using 10 MV photons and were planned for delivery on a Varian Clinac (Varian Medical Systems, Palo Alto, CA) equipped with a 120-leaf Millennium multileaf collimator system, with 40 central leaf pairs of 5 mm and 20 peripheral leaf pairs of 10 mm.

For each patient, 3D-CRT plans with 4 to 6 variably weighted fields were generated. We used 0 to 4 wedges. The IMRT plans were computed using a multiple fixed gantry sliding-window multileaf collimator IMRT technique for delivery. An anisotropic analytical algorithm was used for dose computation with a dose calculation grid of 2.5 mm^3. We used 6 to 9 beams to generate the plans. Beam angles were arranged in a manner according to the tumor and the OAR location for the purpose of achieving maximal target coverage and optimal dose distribution. VMAT plans were generated with 2 simultaneously optimized coplanar volumetric arcs with the same isocenter and with 358° rotation.

Cumulative dose

Deformable registration is an optimization process that can correlate anatomical features observed in 2 different images of the same patient and region. An interactive process is employed to modify the transformation parameters until an optimal match is found between input images.[13] The CT data sets with contours and isodose lines were electronically transferred to the VelocityAI image registration package (Velocity Medical Solution, Atlanta, GA) to determine the cumulative dose delivered during the 2 courses of radiotherapy (original plan and boost plan).

Comparison of techniques

Dose-volume histograms (DVH) for OARs and the PTV were obtained for all patients. The following dosimetric parameters were evaluated and compared amongst treatment planning techniques: D_{mean} (mean dose) and $D_{95\%}$ (the dose received by 95% of the PTV) for the PTV, D_{mean} and V_{30} (the volume receiving 30 Gy or more) for the liver, D_{mean}, V_{15}, and V_{20} (volume receiving more than 15 and 20 Gy, respectively) for the kidneys, and D_{max} (maximum dose) for the spinal cord.

The conformality index (CI) of the plans was defined as the ratio between the volume of the 100% isodose line and the PTV volume. The CIs were calculated for the 2 different treatment courses separately (the large-field and the boost plans). The CI deviation from 1.0 was used for statistical analysis. The volumes of the 25%, 50%, and 90% isodose lines were also obtained. Additionally, the number of MUs per fraction and the estimated treatment time for all the treatment planning techniques were compared. All 2-way comparisons were performed using a paired, 2-sided Student t-test with a significance level of $p < 0.05$.

Results

The tumor and treatment characteristics for all 20 patients are presented in Table 1. Table 2 shows the comparisons for PTV D_{mean}, PTV $D_{95\%}$, CI deviations from 1.0, and MUs delivered per fraction for the 3 treatment techniques.

Table 1
Tumor and treatment characteristics for 20 patients

Age at diagnosis (y)	
Median	64
Range	24 to 84
Histology	
Adenocarcinoma	15
Mucinous adenocarcinoma	3
Infiltrating ductal carcinoma	1
Signet ring cell carcinoma	1
Tumor stage	
IB	2
IIA	3
IIB	10
III	5
Subsite	
Head	13
Tail	1
Body	3
Overlapping	3
Pancreaticoduodenectomy	
Yes	12
No	8
Margins	
Negative	6
Positive	6
CTV volume mean (cm^3)	563
PTV volume mean (cm^3)	787
CTV boost volume mean (cm^3)	193
PTV boost volume mean (cm^3)	309

CTV = clinical target volume.

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