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A COMPARISON OF HELICAL INTENSITY-MODULATED RADIOTHERAPY, INTENSITY-MODULATED RADIOTHERAPY, AND 3D-CONFORMAL RADIATION THERAPY FOR PANCREATIC CANCER

MATTHEW M. POPPE, M.D., VENKAT NARRA, PH.D., NING J. YUE, PH.D., JINGHAO ZHOU, PH.D., CARL NELSON, M.D., and SALMA K. JABBOUR, M.D.

Department of Radiation Oncology, Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT; and Department of Radiation Oncology, The Cancer Institute of New Jersey, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, New Brunswick, NJ

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Abstract—We assessed dosimetric differences in pancreatic cancer radiotherapy *via* helical intensity-modulated radiotherapy (HIMRT), linac-based IMRT, and 3D-conformal radiation therapy (3D-CRT) with regard to successful plan acceptance and dose to critical organs. Dosimetric analysis was performed in 16 pancreatic cases that were planned to 54 Gy; both post-pancreaticoduodenectomy ($n = 8$) and unresected ($n = 8$) cases were compared. Without volume modification, plans met constraints 75% of the time with HIMRT and IMRT and 13% with 3D-CRT. There was no statistically significantly improvement with HIMRT over conventional IMRT in reducing liver V35, stomach V45, or bowel V45. HIMRT offers improved planning target volume (PTV) dose homogeneity compared with IMRT, averaging a lower maximum dose and higher volume receiving the prescription dose (D100). HIMRT showed an increased mean dose over IMRT to bowel and liver. Both HIMRT and IMRT offer a statistically significant improvement over 3D-CRT in lowering dose to liver, stomach, and bowel. The results were similar for both unresected and resected patients. In pancreatic cancer, HIMRT offers improved dose homogeneity over conventional IMRT and several significant benefits to 3D-CRT. Factors to consider before incorporating IMRT into pancreatic cancer therapy are respiratory motion, dose inhomogeneity, and mean dose.

Key Words: **Pancreatic, Tomotherapy, Helical, IMRT.**

INTRODUCTION

In the United States, radiotherapy (RT) is considered a mainstay in the management of pancreatic cancer, both in the adjuvant and definitive settings. The ESPAC trial questioned the importance of adjuvant RT as a result of a reported increase in mortality of patients who received RT.[1, 2] One of the cited weaknesses of the ESPAC trial's RT is that numerous centers performed RT without centralized quality assurance of RT planning.[3] With strict adherence to RT guidelines and careful experienced medical management of these patients during RT, the potential for complications decreases.

Improvements in RT delivery may potentially decrease acute and long-term toxicities, making the rationale for RT in pancreatic cancer more robust and less controversial. Advances in RT delivery with IMRT suggest an improved tolerability over 3D-conformal radiation therapy (3D-CRT) by decreasing doses to critical organs, including stomach and bowel.[4] Ben-Josef *et al.* published results of pancreatic cancer using intensity-modulated radiotherapy (IMRT) to 54 Gy with concurrent capecitabine. Only one patient (7%), experienced a grade 3 toxicity.[5] Multiple techniques for RT delivery in pancreatic cancer have been studied previously, including 3D-CRT, IMRT, and integrated boost IMRT. In a study by Landry *et al.*, IMRT resulted in a reduced dose to small bowel with one-third of small bowel receiving 30.2 ± 12.9 Gy with IMRT *vs.* 38.5 ± 14.2 Gy with 3D-CRT ($p = 0.006$).[6] A dosimetric comparison of 3D-CRT, sequential boost IMRT, and integrated boost IMRT by Brown *et al.* showed that IMRT reduced dose to total kidney V20, small bowel V45, and liver V35. Integrated boost IMRT was further able to lower critical structure dose and permitted dose escalation to 64.8 Gy.[7] Helical IMRT compared with conventional IMRT has been shown to offer a benefit for head and neck malignancy, and may therefore be advantageous for abdominal tumors as well.[8, 9]

This study seeks to evaluate the dosimetric benefit of linac-based conventional IMRT (hereafter, IMRT) and TomoTherapy or helical IMRT (hereafter, HIMRT) for both resected and unresected pancreatic cancer patients in regards to successful plan acceptance and lower dosage to critical structures.

METHODS AND MATERIALS

A dosimetric analysis was performed on pancreatic cancer treatment plans ($n = 16$), both for post-pancreaticoduodenectomy ($n = 8$) and unresected ($n = 8$) pancreatic cancer cases. In postoperative cases, the clinical

Reprint requests to: Salma K. Jabbour, M.D., Department of Radiation Oncology, Cancer Institute of New Jersey, 195 Little Albany Street, Room 2038, New Brunswick, NJ 08903. E-mail: jabbousk@umdnj.edu.

Table 1. Initial inverse planning constraints

Structure	Dose (Gy)	Relative priority
PTV_final	95% >54	100
PTV_final max	59.4	80
PTV_initial	95% >50.4	80
PTV_initial max	59.4	80
Spinal cord max	45	50
Kidney	50% <20	25
Liver	35% <35	20
Stomach	10% <45	20
Bowel	10% <45	20
Liver max	59.4	15
Bowel max	59.4	15
Stomach max	59.4	15
Stomach	1% <45	10
Bowel	1% <45	10

target volume (CTV) was defined as the preoperative gross tumor volume (GTV), anastomotic sites, surgical clips, regional lymph nodes (peripancreatic, hepatoduodenal, and paraaortic), and superior mesenteric artery (SMA)/celiac axes, which creates a volume from approximately T11–L4. In definitive cases, the GTV was defined as disease seen on a diagnostic computed tomography (CT) scan and the CTV also included the regional lymph nodes and SMA/celiac axis. An internal target volume (ITV) was created using a fused inspiration and expiration CT scan of the tumor bed to account for respiratory motion in 3 dimensions. CTV to ITV expansion averaged 5 mm right–left, and 1.5 cm superior–inferior and anterior–posterior, but was individualized for each case. The planning target volume (PTV) was a 5-mm symmetric expansion of the ITV. PTV volumes were found similar to others used in pancreatic dosimetry publications.[7] For cases with unresected pancreatic cancer, the mean initial PTV was 762 cm^3 (482–1303 cm^3), with a mean boost volume (PTV = GTV + 1 cm) 196 cm^3 (75–292 cm^3). For resected, post-pancreaticoduodenectomy cases, the mean PTV was 779 cm^3 (475–1005 cm^3).

PTVs were kept identical with volumes drawn on Eclipse (Varian Medical Systems, Palo Alto, CA) and exported to the TomoTherapy (TomoTherapy, Madison, WI) planning system. Four-field 3D-CRT and 5- to 7-field IMRT plans were generated on Eclipse version 8.2 treatment planning system, using a 5-mm multileaf collimator, with optimization algorithm DVO 8.223 and dose calculation model AAA 8.223. The first 3 unresected cases for IMRT were planned using coplanar beams at the arrangement discretion of the dosimetrist and standardized noncoplanar beam arrangements, per Ben-Josef *et al.*'s publication.[5] We found no significant advantage using noncoplanar beam arrangements and therefore planned all cases with coplanar beams. The first 3 unresected cases for IMRT and 3D-CRT were planned using 6 MV and 15 MV, with and without inhomogeneity correction (IHC) for tissue density, based on CT Hounsfield units (Fig. 1, Table 3). With no significant difference found in engery section and inhomogeneity correction, we elected to compare all 3D-CRT and IMRT plans with 15 MV, IHC off. This is discussed further in our results. TomoTherapy uses a ring gantry and 6-mm multileaf collimator, which rotates in simultaneous motion to the couch, continuously delivering 6-MV photons from all angles around the patient, typically using tens of thousands of beamlets to maximize conformality. We used TomoTherapy version 3.1.2.9 planning system, which by default uses inhomogeneity correction in its dose calculation algorithm.

Unresectable cases were prescribed 50.4 Gy to the PTV1, and 54 Gy to a cone down PTV2 (GTV + 1 cm). This was accomplished concurrently with IMRT and H-IMRT and a 3.6-Gy sequential boost with a 3D plan summation. Postoperative cases were prescribed 54 Gy to a single PTV1 without boost. The dose was normalized on Eclipse, such that the prescription dose covered 95% of the final PTV (PTV1 in post-op and PTV2 in unresected cases). TomoTherapy has no normalization feature but, unlike conventional IMRT and 3D planning, is not required, because the system always achieved the requested PTV coverage in optimization. Inverse planning was weighted in favor of first treating the target volume and then achieving normal organ constraints (Table 1). The relative priorities from Table 1 were used with both Eclipse and TomoTherapy for the initial optimization, with optimization parameters subsequently adjusted to maximize planning goals. Vx is used throughout the analysis to represent the volume receiving 'x,' Gray or greater dose, such that the V45 of the stomach would be the volume of stomach receiving 45 Gy or greater.

The primary goal of the analysis was to determine which treatment planning modality could achieve all components of Table 2 without adjusting the PTV or reducing the prescribed dose. The secondary goal was to determine how low the stomach and small bowel V45 could be reduced without exceeding the other normal organ tolerances, or compromising the minimum PTV dose coverage. Dose volume histogram (DVH) information was directly exported in DICOM format and converted to a spreadsheet for comparison. Intermediate dosage measurements were additionally described with V15 for liver, small bowel, and stomach, and V12 for kidneys. Mean dose was calculated based on volumetric analysis of each organ analyzed.

Table 2. Ideal planning goals

Constraints	Volume limit
Spinal cord	Max dose <45 Gy
Bowel (large and small)	V45 <10%, max. 54 Gy
Stomach	V45 <10%, max. 54 Gy
Kidney (at least one, preferably both)	V20 <50%
Liver	V35 <33%