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Scientific Article

Initial experience with intensity modulated proton therapy for intact, clinically localized pancreas cancer: Clinical implementation, dosimetric analysis, acute treatment-related adverse events, and patient-reported outcomes

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Abstract

Purpose: Pencil-beam scanning intensity modulated proton therapy (IMPT) may allow for an improvement in the therapeutic ratio compared with conventional techniques of radiation therapy delivery for pancreatic cancer. The purpose of this study was to describe the clinical implementation of IMPT for intact and clinically localized pancreatic cancer, perform a matched dosimetric comparison with volumetric modulated arc therapy (VMAT), and report acute adverse event (AE) rates and patient-reported outcomes (PROs) of health-related quality of life.

Methods and materials: Between July 2016 and March 2017, 13 patients with localized pancreatic cancer underwent concurrent capecitabine or 5-fluorouracil-based chemoradiation therapy (CRT) utilizing IMPT to a dose of 50 Gy (radiobiological effectiveness: 1.1). A VMAT plan was generated for each patient to use for dosimetric comparison. Patients were assessed prospectively for AEs and completed PRO questionnaires utilizing the Functional Assessment of Cancer Therapy-Hepatobiliary at baseline and upon completion of CRT.

Results: There was no difference in mean target coverage between IMPT and VMAT ($P > .05$). IMPT offered significant reductions in dose to organs at risk, including the small bowel, duodenum, stomach, large bowel, liver, and kidneys ($P < .05$). All patients completed treatment without radiation therapy breaks. The median weight loss during treatment was 1.6 kg (range, 0.1-5.7 kg). No patients experienced grade ≥3 treatment-related AEs. The median Functional Assessment of Cancer Therapy-Hepatobiliary scores prior to versus at the end of CRT were 142 (range, 113-163) versus 136 (range, 107-173; $P = .18$).

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Conclusions: Pencil-beam scanning IMPT was feasible and offered significant reductions in radiation exposure to multiple gastrointestinal organs at risk. IMPT was associated with no grade ≥3 gastrointestinal AEs and no change in baseline PROs, but the conclusions are limited due to the patient sample size. Further clinical studies are warranted to evaluate whether these dosimetric advantages translate into clinically meaningful benefits.

Introduction

Pancreatic cancer is the fourth leading cause of cancer-related deaths in men and women. At the time of diagnosis, approximately 50% will have clinically localized (ie, nonmetastatic) disease. Treatment paradigms continue to evolve, although concurrent chemoradiation therapy (CRT) is considered a reasonable treatment option after potentially curative resection or for patients with intact borderline resectable or locally advanced unresectable pancreatic cancer, typically after initial treatment with combination chemotherapy.[1-8] CRT may improve margin negative resection rates, lymph node downstaging, and locoregional control in patients undergoing subsequent resection while also offering durable local disease control and palliation of local symptoms for those who are unable to undergo curative resection.

Historical trials evaluating the role of CRT in the management of localized pancreatic cancer have reported acute gastrointestinal (GI) grade 3 adverse event (AE) rates of 70% to 90% and grade ≥4 rates of 40%.[2,4,6,9] However, since that time, improvements have been made in techniques of radiation therapy (RT) delivery, understanding of dose-volume relationships for radiation effects on organs at risk (OAR), and the medical management of symptoms.[10-13]

One potential improvement is the advent of proton beam therapy (PBT) because its unique physical properties (ie, lack of exit dose and lower entrance dose compared with photon RT) allows for a more favorable dose distribution compared with photon RT, with relative sparing of radiation dose to normal tissues, thereby allowing for a theoretical improvement in the therapeutic ratio. However, limited data exist on the role of PBT for the treatment of pancreatic cancer.[14-23] Although demonstrating favorably low rates of GI AEs, the previously reported series have limitations with regard to their inclusion of heterogeneous patient cohorts and treatment techniques, lack of technical treatment details, lack of comparative dosimetric data with advanced photon-based techniques, and use of passive scatter PBT as opposed to more advanced pencil-beam scanning (PBS)/intensity modulated proton therapy (IMPT) techniques.

The purpose of this study was to describe the clinical implementation of PBS-IMPT for the treatment of intact, clinically localized pancreatic cancer. We report a detailed description of treatment planning techniques and a matched dosimetric comparison of PBS-IMPT with volumetric modulated arc therapy (VMAT). We also report acute AE rates and patient-reported outcomes (PROs) of health-related quality of life (HRQoL). We hypothesized that IMPT would result in improved OAR-sparing compared with VMAT and would be associated with favorable acute treatment tolerance.

Methods and materials

Patients

This was a retrospective review of the first 13 consecutive patients with intact, clinically localized pancreatic adenocarcinoma who received IMPT with concurrent chemotherapy (capecitabine 825 mg/m^2 twice daily [n = 11] or continuous venous infusion 5-fluorouracil 225 mg/m^2 for 5 days per week during RT [n = 2]) at our institution between July 2016 and March 2017. Patients were chosen for treatment with IMPT on the basis of insurance coverage of IMPT and physician/patient preferences. The institutional review board approved the conduct of this study.

Simulation and treatment setup

Patients were instructed to fast for at least 2 hours prior to simulation and treatment. Oral contrast was not administered. Patients were positioned supine with their arms above their head in a Vac-Lok (CIVCO Radiotherapy, Coralville, IA) or Alpha Cradle (Smithers Medical Products, Inc., North Canton, OH) custom immobilization device on a CIVCO couch (CIVCO Radiotherapy, Coralville, IA). A noncontrast, free-breathing, 4-dimensional computed tomography (CT) scan was obtained. Additionally, an intravenous contrast-enhanced scan was obtained if there were no contraindications.

Intensity modulated proton therapy planning

CT images and structures were imported into the Eclipse Treatment Planning System (Version 13.7, Varian Medical Systems, Inc., Palo Alto, CA) for treatment planning. Plans were generated on the average series of the 4-dimensional CT scans. The amplitude of tumor motion