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Using Stereotactic Body Radiotherapy (SBRT) for Pancreas Cancer: Adjuvant therapy (AT), Intensity Modulated Radiation Therapy (IMRT) and Case Examples

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Abstracts: In America, pancreatic cancer ranks as the fourth most common killer. A dismal outlook awaits patients diagnosed with pancreatic cancer. When diagnosed, most individuals have tumours that cannot be removed. The clinical experience with stereotactic body radiation (SBRT) for pancreatic cancer has demonstrated excellent local control, which is very encouraging. Intensive systemic chemotherapy can be maintained during SBRT's brief treatment duration, which is a major benefit. Pancreatic adenocarcinoma patients have just one curative therapy option, and that is surgery. Rates of local recurrence and/or distant metastases are still high, leading to poor long-term results, even when patients who are considered resectable undergo rigors surgical care. Patients who have undergone resection have been the focus of research into adjuvant therapies (ATs), which include chemotherapy and chemoradiation therapy (CRT), with the goal of improving survival rates and reducing recurrence rates. Evidence for adjuvant radiation therapy (RT) is inconsistent, in contrast to that for adjuvant chemotherapy, which consistently improves results. Radiation has shown promise in improving local control, but this has not necessarily translated into better survival rates for patients. Limitations in generalizability stem from early trials' use of less-than-ideal radiation methods. More optimised RT techniques are being used in recent and continuing trials to elucidate its significance in therapeutic strategies. New radiation methods are also being studied, including stereotactic body RT (SBRT) and intensity modulated RT (IMRT). These efforts are being made in the hopes that they may decrease toxicity rates and enhance disease-related outcomes. Controversy surrounds adjuvant RT's function. Due to their use of what is now known as sub-optimal RT, early trials were defective and had inconsistent outcomes. Current RTOG 08-48 and other adjuvant RT trials use evidence-based volume targets and strict quality control measures. The function of adjuvant radiation in patients with resected PC will be better understood based on the findings of this research. The potential for increasing the therapeutic window and bettering disease outcomes is held by the incorporation of contemporary radiation techniques like SBRT and IMRT, which maximise dosage to target volumes while minimising dose to normal tissues.
Keywords: Stereotactic Body Radiotherapy (SBRT), Pancreas Cancer: Adjuvant therapy (AT), (IMRT).

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Introduction

In the US, pancreatic cancer ranks as the fourth most deadly malignancy. Overall survival (OS) at 5 years is below 5% for all patients. Even after surgery, the prognosis is not good. However, R0 resection surgery remains the gold standard for curative treatment. Because most patients are considered unresectable upon diagnosis, researchers have opted to use chemotherapy and radiation therapy as a treatment option. Research has demonstrated that patients with locally advanced unresectable pancreatic cancer who get radiation therapy in addition to 5-fluorouracil (5FU) had a better chance of survival than those who have radiation therapy or chemotherapy alone [1, 2]. Patients with locally advanced pancreatic cancer were randomly assigned to receive either gemcitabine alone or gemcitabine with concurrent radiation in a recent study by the Eastern Cooperative Oncology Group (ECOG). Other trials that have investigated the benefits of chemoradiotherapy have not demonstrated any benefit when radiation therapy is added to chemotherapy. When comparing individuals treated with gemcitabine alone to those treated concurrently with radiation, this study found that the latter group had a better chance of survival. Chemoradiotherapy has the potential to increase overall survival in patients whose illness has stabilised after chemotherapy. Although disease-related deaths mostly occur in the system, local progression does cause a lot of pain and reduces people's quality of life. Thirty percent of the 76 individuals tested positive for locally destructive disease at death, with no signs of distant progression, according to an autopsy series conducted at Johns Hopkins University. The prevalence of locally destructive pancreatic cancer was strongly associated with DPC4 immunostaining in these tumours. Based on these findings, it appears that a key therapeutic aim for some patients is the management of local pancreatic progression. Consequently, radiation therapy has the ability to enhance patient survival rates while also playing a crucial role in local control. One promising new approach to radiation treatment is stereotactic body radiotherapy, or SBRT [3-5]. By skipping lengthy treatment periods in patients with a low life expectancy, SBRT is able to manage localised illness and alleviate symptoms in a shorter delivery time, which is a significant advantage over standard fractionated radiation therapy. Additionally, in contrast to traditional fractionated radiation therapy schedules, the reduced treatment time permits continuous full-dose chemotherapy with minimum interruption. Radiation oncology has come a long way, with innovations like four-dimensional (4D) computed tomography (CT) and daily onboard imaging enabling smaller treatment margins, which means more doses delivered to conformal targets and less to vital normal structures. Our SBRT approach for locally advanced pancreatic cancer at Stanford University has improved local control outcomes when compared to previous series. Since its inception,

Selecting Patients

Patients can't be guaranteed SBRT unless certain conditions are met. In a perfect world, the patient would have locally advanced cancer that is either completely or partially unresectable, and there would be no involvement of clinical lymph nodes or distant metastasis. It is suggested for tumour sizes less than or equal to 5 cm, while there is no exact size threshold. Anatomical factors pertaining to vital organs (especially the stomach and duodenum) are also significant in the selecting process. It is preferable for tumours to have fewer normal stomach and duodenal next to them. Researchers at Beth Israel Deaconess Medical Centre did in fact come up with a risk-adapted dosage strategy that takes duodenal proximity into account [6-9]. The natural history of the disease can be better understood with an initial course of systemic therapy in patients with significantly elevated tumour markers or with suspicious but indeterminate lesions in the liver or other organs, as many of these patients are at risk of distant progression.

Important Details

Movement of the Tumour and Gold Fiducial Seeds

Treatment planning and delivery must take into consideration the complicated motion of the upper abdominal organs, especially the pancreas, because of its proximity to the diaphragm. Pancreatic tumours can migrate 2-3 cm in the superior-inferior (SI) direction with normal breathing. Researchers found that patients with pancreatic cancer who underwent CyberKnife SBRT experienced substantial pancreatic displacement in three different directions: SI (mean up to 12.7 mm), left-right (mean up to 9.4 mm), and anterior-posterior (mean up to 5.5 mm). To avoid increasing normal tissue toxicity and ensure enough margins to avoid "marginal misses," the clinician must understand the extent to which the tumour is moving before expanding the tumour volume. This expansion may be reduced or non-uniform. Our method does this by increasing the precision of targeting and setup by tracking the tumour with three to five gold

fiducial seeds implanted into or near it [10, 11]. We usually place seeds by endoscopy, but other methods such as CT guidance, laparoscopy, laparotomy, or during a surgical effort at resection can also be used. The effect of seed movement can be reduced by doing this technique at least five days before scanning the treatment-planning simulation.

Therapy Routines

Supine with arms raised over head, patients undergo simulated treatments. An Alpha Cradle, manufactured by Smithers Medical Products in North Canton, OH, is used to immobilise them. At 1.25 mm cuts, a CT scan is taken using an intravenous contrast-enhanced arterial and venous (biphasic) pancreas protocol. It is common practice to obtain arterial phase scans while the patient is exhaling. Before the scan, patients are asked to fast for 8 hours. No oral contrast will be administered. A simulated scan that includes 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) can help with target definition and detect hidden metastases. Furthermore, a 4D-CT scan is carried out and breathing phases are recreated with the help of the Varian Real-Time Position Management system (RPM, Varian Medical Systems, Palo Alto, CA). The GTV is best observed as a hypodense lesion in the early arterial phase and is contoured on the axial slices of the biphasic CT. When contouring, uptake on the FDG-PET scan is helpful for defining the tumor's extent. In order to compensate for tumour deformation, the fiducial seeds serve as registration locations for fusing the end-inhalation and exhalation phases of the 4D-CT scans during the respiratory tracking on the CyberKnife (Accuray, Sunnyvale, CA) treatment. The 4D-CT scan phases that covered the gating window were chosen and fused to the treatment-planning scan using DICOM coordinates when respiratory-gated treatment administration was used. Visual analysis of the pancreatic tumor's movements through the respiratory cycle shown on the 4D-CT is used to choose the gating window, which is centred around the end-expiration phase [12-15]. By modifying the GTV to account for tumour position changes as shown on the 4D-CT phases that represent the gating window, the internal target volume (ITV) can be calculated. The ITV + two or three millimetres to account for setup error is called the planning treatment volume (PTV). Nodes in the surrounding areas are not accounted for in the target volume. The treatment also included the projection of fiducial markers onto the fluoroscopic pictures, which were contoured.

Drug Schedule

Our first investigations used a dose of 25 Gy delivered in a single fraction to the isodose line, which covered 95% of the target. Limits were imposed on the duodenum and stomach dose with the utmost priority, following normal tissue limits for the liver, kidneys, spinal cord, stomach, and other intestines. In addition, the 50% isodose line must not extend beyond the lumen's distal, non-adjacent wall. Presently, we recommend 33 Gy delivered in 5 fractions through gated RapidArc or traditional step-and-shoot IMRT. Table shows the normal tissue limits that should be considered when planning the treatment .

Administration of Therapy

In the beginning, we used the CyberKnife to administer SBRT with the help of the Synchrony (Accuray Inc.) respiratory tracking system. The imaging system takes digital radiographic pictures of the patient in real time using two X-ray sources mounted on the ceiling and amorphous silicon detectors. The Synchrony respiratory tracking device constantly updates a correlation model that links the patient's fiducial movement to the LEDs implanted on their chest wall. With this model, the tumor's respiration may be monitored in near real-time. We have also experimented with standard linear accelerator delivery methods, such as the TrilogyTM and TrueBeamTM linear accelerators manufactured by Varian of Palo Alto, CA. Orthogonal kilovoltage pictures are utilised to align to bony architecture on the day of treatment, before radiation delivery. CBCT, or cone-beam computed tomography, is sometimes also utilised for this purpose. Fluoroscopic pictures are taken in both the anterior and posterior positions after initial alignment [16, 17]. These images include an overlay of the fiducial ITV's position from the digitally reconstructed radiograph (DRR), which includes both the fiducial area and a little margin of 2-3 mm. In order to ensure that the radiation beam is "on" when the fiducials enter the fiducial ITV and "off" when the seeds escape, this phase involves adjusting the gating window and aligning the fiducial seeds. This alignment is done as the patient progresses through the respiratory cycle . The administration of the treatment follows confirmation. To ensure the implanted fiducials are in the correct place, orthogonal kV pictures are acquired at the start of the gated phase during treatment.

Treatment of Pancreatic Cancer with SBRT

Within a single fraction, fifteen patients with locally advanced pancreatic cancer were administered doses of 15, 20, or 25 Gy as part of a Phase I dose escalation research conducted at Stanford. The experiment was terminated before reaching the maximum tolerated dose since the primary clinical end point of local control was reached at 25 Gy. There was complete local control at the time of death or last follow-up, and the median OS was 11 months. After that, in 2005, Koong et al. performed a Phase II research that involved traditional fractionated radiotherapy with IMRT and CyberKnife SBRT boost to the main tumour. The patient had IMRT to 45 Gy along with concurrent 5FU or capecitabine treatment for the primary tumour and regional lymph nodes. Subsequently, an SBRT boost of 25 Gy in a single fraction was administered to the primary tumour. The 94% local control rate and 33 weeks of median overall survival were not unexpected. Grade 3 gastrointestinal (GI) toxicity occurred in two patients, while grade 2 GI toxicity occurred in four patients. Gemcitabine chemotherapy was incorporated into the treatment plan due to elevated toxicity and advancement of systemic illness. A Phase II trial examined the use of 25 Gy SBRT in between full-dose 1,000 mg/m2 gemcitabine treatment. The median survival time was 11.4 months, and 19% of the patients experienced local progression as a component of their progression (Schellenberg et al. 2008). Although the risk of duodenal ulcers was higher with SBRT, the survival rate was similar to that of traditional chemo [16-19]. Five patients experienced intestinal ulcers of grade 2, one patient had stenosis of grade 3, and one patient had a perforation of grade 4. A pooled retrospective examination of seventy-seven patients who had 25 Gy SBRT was performed by Chang et al. The majority of patients (96%) underwent chemotherapy, with gemcitabine being the most common kind. OS was 21% and 84% free of local progression after one year. Regardless of whether the tumour was located in the head or uncinate or the body or tail, the rate of 1-year independence from local progression was the same. From the time of diagnosis, the median OS was 11.9 months. Some patients in this series had already had chemotherapy and/or radiation, making it impossible to compare the OS rate to other research. Grade 2 or higher acute toxicity was experienced by 5 patients, while grade 2 or higher late toxicity was experienced by 13 patients. Among the patients, 10 developed ulcers in the small intestine or stomach, 3 experienced biliary stricture, 1 had duodenal stricture, and 1 had duodenal perforation. According to Chang et al. (2009), the actuarial rates of Cgrade 2 toxicity at 6 months were 11% and at 12 months it was 25%. For pancreatic cancer patients with localised metastases, the standard linear accelerator is now the treatment of choice for SBRT. Research conducted by Schellenberg et al. documented the success of TrilogyTM in treating locally advanced pancreatic cancer at Stanford University utilising a single fraction of 25 Gy. Repeating the results of the prior CyberKnife procedure, the rate of independence from local progression after one year was 94%. Our previous data showed a median survival of 11.8 months. The toxicity remained unchanged regardless of the SBRT delivery equipment.

Reports from Other Academic Centres

As a component of failure, 27% of the 22 patients studied by Hoyer et al. (2005) experienced local progression; however, only 1 patient exhibited isolated local tumour advancement. There was a lot of gastrointestinal harm, according to the researchers. But that's probably because our patients at Stanford University were exposed to smaller fields of radiation. Results from 39 patients with locally advanced, unresectable pancreatic cancer who underwent CyberKnife surgery are detailed in a recent study by Mahadevan et al. After the first two gemcitabine rounds, patients were restaged. Patients who had disease stability underwent an extra chemotherapy round, during which they were administered 24-36 Gy in three fractions. The dosage was adjusted according to the pancreas's connection to the duodenum [20-23]. The level of control at the local level was 85%. Three individuals experienced toxicity of late grade 3. With 24-36 Gy in 3 parts, Mahadevan et al. (2010) found 78% local control in a previous sample of 36 patients. Based on their findings, SBRT has the potential to treat locally advanced pancreatic cancer with low interference from chemotherapy and acceptable side effects. Research conducted by Rwigema et al. at the University of Pittsburgh examined the results of seventy-one pancreatic cancer patients who underwent SBRT. The median dose administered to patients was 24 Gy, with a range of 18-25 Gy. While 94% of patients underwent SBRT with a single fraction, 6% underwent fractionated SBRT with two or three fractions up to twenty to twenty-four Gy. Tumours less than 15 mL had a local control rate of 77%, while tumours greater than 15 mL had a rate of 58%. Complete pain alleviation was reported by thirteen out of sixteen individuals following SBRT. As a result of SBRT, no patient suffered a bowel perforation. Three fractions of 30 Gy were administered to twenty-three patients with locally

advanced pancreatic cancer in an Italian study. There was local advancement in four patients, whereas nineteen experienced a partial response, full response, or stable illness. There were statistically significant impacts of nodal metastases, treatment response, and surgical resection on survival and quality of life, according to multivariate analysis. Didolkar et al. (2010) evaluated the effects of administering 15-30 Gy in 3 fractions to 85 patients with unresectable pancreatic tumours. The median duration of response for the 78 individuals was 8 months, with some seeing partial response, stable disease, or a full response. Nineteen patients experienced toxicity at the grade III or IV level, which manifested as gastritis, duodenitis, diarrhoea, and renal failure.

A Historical and contemporary overview of adjuvant radiation treatment for pancreatic cancer

Imaging examinations like as CT scans, MRIs, and endoscopic ultrasounds are used in a prospective evaluation to determine resectability. A case of resectable disease is one in which no distant metastases have spread and no nearby vasculature (such as the celiac axis, hepatic artery, superior mesenteric artery, superior mesenteric vein, or portal vein) has been involved. Even though it's a subjective category that might vary among surgeons and institutions, borderline resectable illness encompasses lesions with minimal SMA abutment (<180°), venous involvement (PV or SMV) that is considered resectable, and situations where reconstruction is feasible. The sole therapeutic option for patients with PC that has the ability to cure the disease is surgery [24-27]. The percentage of people whose illness can be surgically removed is around 20%. High rates of local (50-90%) and distant (peritoneal: 20-35%; liver: 20-90%) recurrence restrict results for this group of patients, even though it is possible to remove all gross disease. A major cause of morbidity (such as discomfort, ulceration, bleeding, blockage, and cholangitis) is local recurrence. In addition, distant failure and consequent fatality are common outcomes of uncontrolled local disease. In an effort to improve long-term results and decrease recurrence rates, CRT and other adjuvant treatments (ATs) have been the subject of much investigation .

Treatment after pancreatic cancer removal (AT)

There have been a lot of research looking at the effectiveness of ATs in an effort to help these patients. There are several limitations in the interpretation and generalizability of the early studies that looked at AT for resected PC because to problems with the study designs and analyses. As an example, when determining resectability initially, many did not incorporate pre-operative imaging. One example is stereotactic body RT (SBRT), in addition to intensity modulated RT (IMRT). The radiation oncologist must first outline the target volumes and any organs that could be at danger in inverse planning before IMRT can begin, unlike in 3-dimensional conformal RT. The next step is to optimise the treatment plan according to the volumetric and dosimetric restrictions (i.e., radiation prescription) for the target volumes and the organs that are at risk. Interim radiation therapy (IMRT) uses tiny "beamlets" to treat radiation instead of a larger blanket. It can be used in two ways: either as "step and shoot" IMRT, where the radiation beam changes shape while the machine is off, or as dynamic IMRT, where the collimating leaves move in and out of the beam path during treatment [28-31]. The end result is a substantial decrease in doses to nearby normal tissues as the prescribed dosage conforms to the specified target volumes .

The combination of high doses of ionising radiation with a high level of anatomic targeting accuracy and reproducibility is achieved by stereotactic body RT, which goes by several names: SABR, HIGRT, and others. This way, the target cells will be killed off as effectively as possible with minimal harm to nearby healthy tissues. To compensate for daily changes in target volume and neighbouring normal tissue placement, SBRT and IMRT both use stringent imaging guidance. There are two main advantages that could be gained by a reduced RT duration. To begin, the physiologically effective dosage is believed to rise with increasing fractional doses of radiation according to radiobiological principles. Secondly, patients will be able to go on to systemic medications more rapidly if the total therapy period is substantially reduced. Precise volume delineation of targets is a cornerstone of these conformal radiation procedures .

This calls for an in-depth familiarity with typical anatomy as well as lymphatic drainage patterns. In addition to surgical and pathologic factors, preoperative tumour characteristics as identified by preoperative imaging must also be carefully considered for accurate target volume delineation. The RTOG published contouring rules to standardise this technique, and they are now part of the RTOG 0848 protocol. Considerations such as tumour location prior to surgery, surgical anastomoses, and nodal regions determined by vasculature all go into the suggested outlines. Researchers

from Johns Hopkins and the University of Maryland have joined forces to create target volumes by analysing failure patterns in 202 patients who have had cancer removed .

Results from IMRT clinical trials

As it pertains to PC, IMRT has been used in adjuvant and locally advanced settings. These series should only be used for toxicity evaluations and feasibility studies due to the minimal patient numbers. Initial results from a multi-group study including patients with resected disease (n=8), unresectable disease (n=13), and unresected recurrence (n=3) were published by the University of Chicago in their first report using IMRT with concurrent 5-FU. Six acute and one late grade 3 or 4 non-hematologic toxicity occurred during the course of the treatment, which was generally well-tolerated. The median follow-up period was fourteen months. Despite the limited sample size, after a median of 17 months of follow-up, none of the eight patients who had resection had a local recurrence. University of Michigan researchers studied the effects of concurrent gemcitabine and dose-escalated IMRT (up to 60 Gy) in a phase I/II prospective trial. Radiation was focused on the most severe cases in their 50-patient series, with individualised margins that allowed for precise targeting of the respiratory system [32-35]. To optimise local and distant control, full dose gemcitabine (1,000 mg/m2) was administered concurrently. It should be noted that previous research assessed the unacceptable toxicity of full dose gemcitabine administered concurrently with RT. The present research tested the hypothesis that IMRT could lessen the radiation to healthy tissues, making this method safer. **Figure 1 and 2**

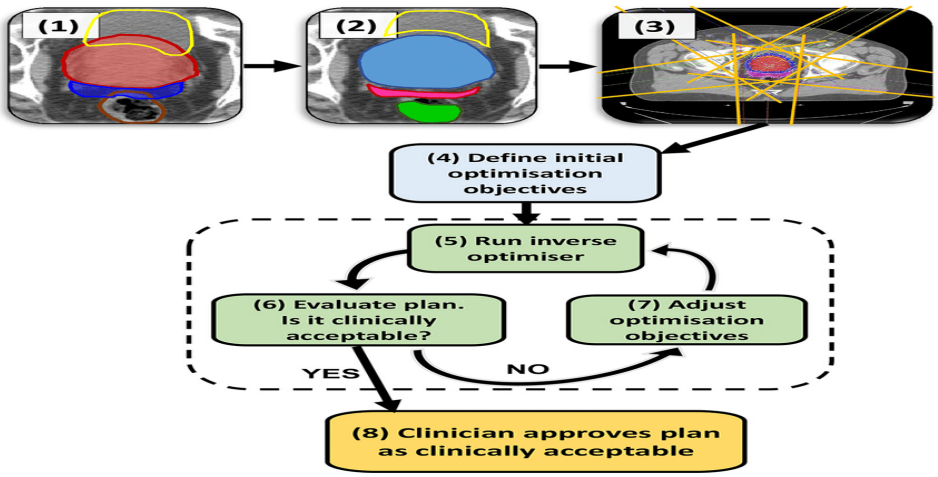

Figure 1. A typical manual IMRT treatment planning pathway.

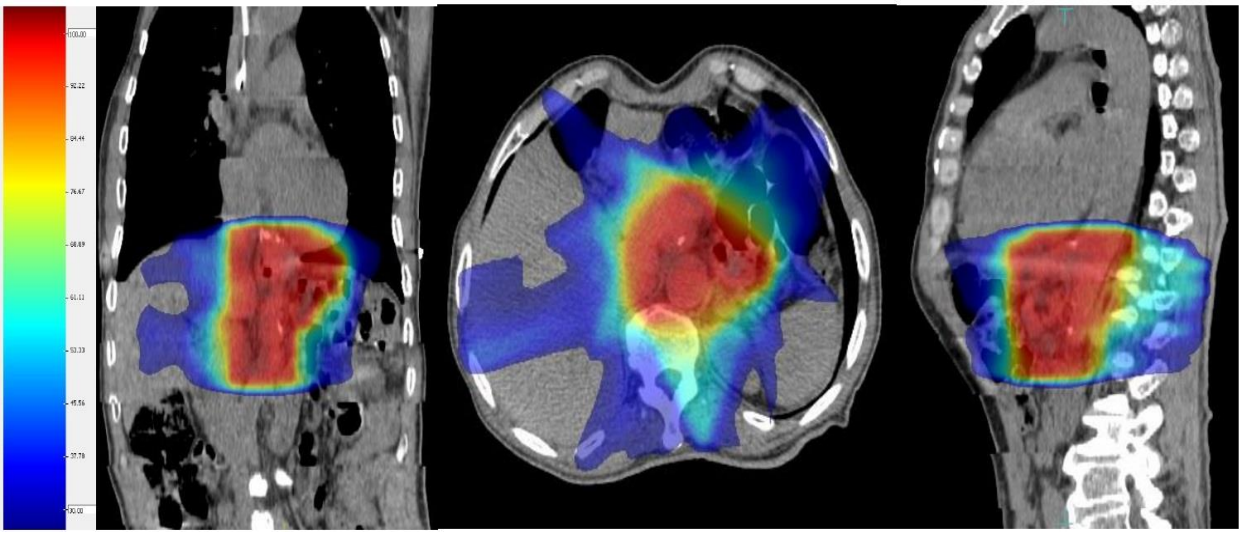

Figure 2. A retrospective dose-evaluation and clinical analysis of intensity-modulated radiation therapy (IMRT) for adjuvant treatment of resected gastric cancer.

Toxicity

The main organs that limit the dose of SBRT when considering it for pancreatic cancer is the nearby duodenum and stomach. It is inevitable to irradiate parts of these vital structures because of how near they are to the main tumour. In order to determine the duodenal toxicity effects of SBRT, Murphy et al. examined the results of seventy-three individuals who had never been exposed to radiation before and were given 25 Gy in a single portion at Stanford University. In relation to the volume irradiated by SBRT, 12 patients (16.4%) encountered grade 2 or greater toxicity. At 12 months, the development of Grade 2-4 toxicity was associated with the V10, V15, V20, and V25 (the volume in cm3 that received 10 Gy or more) [36-39], according to Murphy et al. (2010). According to Murphy et al. (2010), there was a 29% actuarial risk of grade 2-4 toxicity after one year, but the authors discovered that duodenal toxicity was greatly reduced when V15\9.1 cm3, V20\3.3 cm3, and Dmax\23 Gy were maintained. Ulceration was the most prevalent side effect. These findings validate that the toxicity risk is dose-and volume-dependent, and they are the first to describe duodenal tolerance within the context of SBRT. This information is relevant for SBRT with a single fraction, but it doesn't cover courses with more than one fraction.

Examples of Cases 1 The patient was a 54-year-old female who had lost 10 pounds, experienced jaundice, and was in severe stomach pain. She had a cholecystectomy after an abdominal scan and endoscopy confirmed gallbladder illness. It was unclear what was causing her jaundice, so she had a CT scan of her pancreas performed. The results revealed a hypodense lesion in the pancreatic head, with just a small amount of involvement of the superior mesenteric vein (SMV). Jaundice cleared up after she had a second ERCP with a stent implanted. Adenocarcinoma of the pancreas was discovered during an endoscopic ultrasound-guided biopsy. She began gemcitabine chemotherapy after receiving the diagnosis of borderline resectable pancreatic cancer. According to CA 19-9, the value was 34. She was considered to be an excellent SBRT candidate. Following a single chemotherapy cycle, she underwent a treatment of SBRT to her pancreas tumour, which consisted of 33 Gy delivered in 5 fractions by a respiratory gated arc method on an IGRT enabled linear accelerator.

Despite enduring brief episodes of grade 1 nausea, she managed to endure her radiation treatment well. Gemcitabine treatment was continued one week following the end of her SBRT. After one month of SBRT, her major pancreatic tumour shrank slightly, according to a CT scan. An oncologic surgeon examined her and broached the subject of final surgical excision with portal vein repair during their consultation. She had a Whipple pancreaticuoduodenectomy with portal vein repair around six weeks after SBRT ended because exploratory laparotomy did not reveal any metastasis. The final pathology report showed that 0 out of 14 lymph nodes were involved with a well-differentiated T2 N0 tumour. Post-operative alterations were seen on a CT scan taken three weeks after surgery, but no symptoms of illness recurrence were detected. Gemcitabine chemotherapy was resumed by her. She went through four more rounds of chemotherapy [40-43]. A CT scan revealed no obvious indications of residual or recurrent disease at her 6-month follow-up, and her CA 19-9 was 8 (within normal limits). An epigastric ache, gas, and loss of appetite were the symptoms experienced by a 54-year-old male patient. A 3.7 cm hypovascular tumour around the superior mesenteric artery (SMA) and occlusive to the SMV was shown by a computed tomography (CT) scan, which was located in the pancreatic uncinate process. The diagnosis was adenocarcinoma, as confirmed by biopsy. Present upon diagnosis was a CA 19-9 of 3294. Before transitioning to a dose-reduced chemotherapy regimen consisting of oxaliplatin, irinotecan, fluorouracil, and leucovorin (FOLFIRINOX), he started chemotherapy with gemcitabine and erlotinib. Using a decreased dosage of FOLFIRINOX, he went through six cycles. A restaging computed tomography (CT) scan of the pancreas showed a stable mass measuring 3.7 by 9.0 cm that was still enclosing the SMA and blocking the SMV. The CA 19-9 code was 79. An SBRT regimen was suggested after reviewing his case by a multi-modality tumour board. The subject was simulated after having fiducial seeds implanted. His pancreatic mass was treated with 33 Gy of SBRT over 5 fractions utilising 10MV photons on an IGRT-enabled linear accelerator using a respiratory gated arc method. Without experiencing any severe toxicities, he finished his medication in just five consecutive days. The patient reported feeling well at the 6-month follow-up following SBRT, with no gastrointestinal effects reported. At this stage, the CT scan revealed a primary tumour that was stable and did not indicate any signs of recurrence or metastasis. The third case The patient was a 69-year-old lady who complained of abdominal distention. A computed tomography (CT) scan of the pancreatic ucinate process, which includes the SMA [44, 45], showed a 2.5 9 2.6 cm mass. Pancreatic cancer was diagnosed using fine needle aspiration. The temperature of CA19-9 was 45 degrees. By

utilising a linac-based technique, she was able to administer 25 Gy of SBRT to her locally progressed pancreatic tumour in a single fraction (Figure 3).

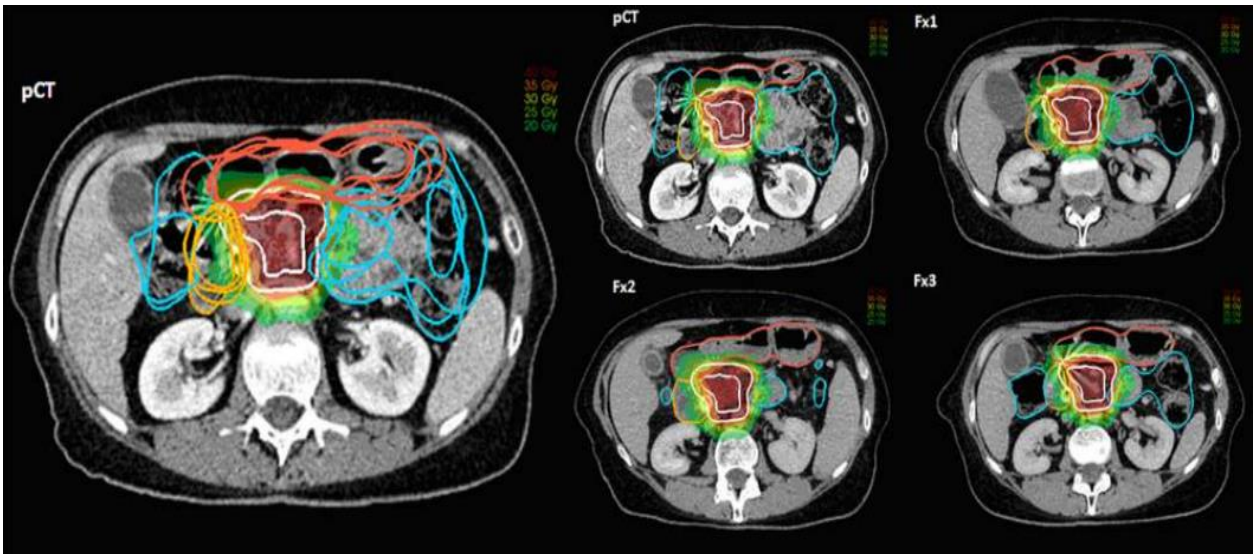

Figure 3. Left: The effect of individual differences in anatomy on the dosage and course of treatment. In order to evaluate changes in the V35 region, daily CT outlines were rigidly projected onto the pCT scan with respect to the tumour site.

A respiratory gated IMRT scheme was used to treat her. With no treatment interruptions or acute toxicity, she finished her course of medication. Once her radiation treatment was over, she got back to her gemcitabine chemotherapy. No lymphadenopathy or distant metastases were detected on her first PET scan, which was conducted six weeks following therapy [46, 47]. The results demonstrated an interval decrease of FDG uptake in the pancreas. With the SMA still encased, a pancreatic protocol CT showed no change to the pancreatic mass. The tumour not only bordered the celiac artery but also constricted the hepatic artery. Afterwards, PET scans revealed no FDG activity in the pancreatic tumour, and CT scans every three months for the first year came back stable. Metabolically active disease was not detected in a PET scan conducted during the 2-year follow-up. Three years later, a computed tomography (CT) scan revealed a stable pancreatic mass encasing the SMA, as well as constriction of the left hepatic artery and splenic-portal venous confluence. There was no abnormality in CA 19-9. After finishing SBRT 3.5 years ago, she is still doing OK at her most recent follow-up.

Conclusion

For diseases that can be surgically removed, surgery remains the gold standard of treatment. Although SBRT has demonstrated encouraging local control in clinical trials for unresectable pancreatic cancer, no substantial improvements in patient survival have been noted. Radiation treatment has the potential to make some individuals whose tumours were previously considered borderline or unresectable resectable. Because systemic spread is likely to occur in the majority of patients, the idea of combining SBRT with optimised chemotherapy is crucial. Because local progression might affect these patients' quality of life and mortality, patients whose illness is stable or well controlled with systemic therapy may benefit from a course of SBRT to the tumour bed for local control. Even in cases of metastatic disease, SBRT should be thought of for the palliation of symptoms associated with local progression. When diagnosing individuals with locally advanced cancer, we recommend systemic chemotherapy for two to four months. Imaging studies can then be used to gauge the treatment's efficacy. When the patient's condition is stable or improving, SBRT should be investigated. A recent German study suggested this method, showing that radiation can help patients whose systemic illness has not progressed during the first three to six months of gemcitabine chemotherapy. How SBRT can be most effectively used with more aggressive and potentially harmful chemotherapy treatments like FOLFIRINOX needs more research. We still don't know how to best combine SBRT with systemic chemotherapy. Also, since we know how well the bowels tolerate hypofractionated radiation, we may be able to use this information to develop a risk-adapted fractionation plan that takes intestinal toxicity into account.

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