8-9-2022

Deep Inspiration and End Exhale Breathhold Evaluation for the Treatment of Locally Advanced Pancreatic Adenocarcinoma using the ViewRay MRIdian LinacTM

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Graduate Medical Dosimetry Program

Abstract

Introduction

Radiation therapy has been limited in the treatment of locally advanced pancreatic cancer. This is due to the dose tolerance to nearby organs at risk and breathing motion. Advancements in radiation treatment technology have now allowed pancreatic patients to be treated to higher doses in fewer fractions using stereotactic body radiotherapy treatment. With the use of MRI-guided treatments, using the ViewRay MRIdian linac, doses can be escalated using online adaptive treatment planning and real time tracking. However, there has yet to be an optimal breathhold technique investigated that can aid in this process.

Methods

Five patients that had been previously treated on the institutions ViewRay MRIdian linac to the pancreas were evaluated. A deep inspiration and end exhale plan were created for each patient using the ViewRay TPS. The treatment goals followed the SMART trial protocol guidelines. The prescription was 50 Gy treated in 5 f(x)s at least every other day. CTV goal coverage was 100% of the volume to 95% of the prescription dose and luminal OARs (stomach, duodenum, small intestine, and large intestine) to not exceed 33 Gy to 0.5 cc. A step and shoot intensity modulated radiation therapy technique was used.

Results

A nonparametric sign test was performed, and there was no statistically significant difference in the coverage of the CTV by the 95% isodose line. There was also no significant data found in the volume of the duodenum or stomach that received 33 Gy to 0.5 cc or the volume of the two organs within the zPTV_PRV30 planning ring.

Conclusion

An optimal gating technique was not discovered. A larger study group and further research is necessary to produce significant data.

Introduction

Pancreatic cancer is slowly becoming a common cause of cancer mortality, it is projected that it will become the second leading cause of cancer death in the United States.[1] The only chance for cure of this disease is surgical resection. However, 80-85% of patients that present with pancreatic cancer often present with advanced disease and are not surgical candidates, leading to a 5-year survival rate of ~10%. Even with surgical resection the prognosis is dim with approximately 20% surviving at 5-years.[1]

Most pancreatic cancers are adenocarcinomas and are located in the pancreatic head. Due to this location one common symptom is jaundice due to the blockage of the nearby biliary duct.[1] Other symptoms may include abdominal pain, nausea or vomiting, indigestion, back pain, changes in stool consistency and/or weight loss. These vague symptoms can lead to a delay in diagnosis adding to the reason of why these patients are often diagnosed at a later stage of disease, some patients have no symptoms at all. The first stage of diagnosis is with a diagnostic computed tomography (CT) scan. The scan can delineate between the hypodense cancer tissue and the pancreas.[1] A CT alone may tell whether or not a tumor is resectable by showing local tumor extension.[2] A magnetic resonance image (MRI) may also be used to help visualize possible liver metastases, and an endoscopic ultrasound which can be used to identify lymph nodes and nearby vascular structures.[1] When the dismal prognosis is given patients are then placed into different categories for staging; resectable, borderline resectable, locally advanced, and metastatic.[1]

Unfortunately, treatment options for pancreatic cancer are limited and even though surgery is the only cure there is still a high rate of recurrence post surgery.[2] When adding chemotherapy and radiation (CRT) post surgery the survival rates almost double from 10.9 months to 21 months.[2]

Preoperative CRT has yet to be established as a treatment standard but is being used more and more for resectable and borderline resectable disease.[1,2] Studies are currently being completed comparing these two treatment techniques.[1] For unresectable disease, patients can receive CRT or more commonly chemotherapy alone.[2] Chemotherapy alone is often the treatment modality used for widely metastatic disease, however, radiation can also be used to palliate symptomatic disease.[1,2]

For neoadjuvant and adjuvant radiation therapy the simulation technique for treating pancreatic cancer is the same. Patients are simulated in the supine position with the standard being arms supported up over the head. This allows the arm to be outside of the treatment field.[2] If patients cannot maintain the arms up position and their arms are down by their side they will have to be avoided while planning so that the arms are not in the treatment fields. Contrast can be used both orally and intravenously to delineate the duodenum and vascular landmarks.[2] Because the pancreas lies just below the diaphragm motion can affect the imaging and treatment process. To account for this a 4D computed tomography scan can be used for simulation. A 4DCT scan acquires images at different breathing phases and will show the movement of the pancreas and aid in treatment planning.[2] Another option to limit motion is through the use of respiratory gating by either having a patient hold their breath at the top, inspiration breath hold, or the bottom, exhalation breath hold.

Breathing motion is one of the greatest downfalls in treating upper abdominal cancers with radiation therapy. Continual motion from breathing is not the only limiting factor but also normal involuntary motion, such as peristalsis and motion of gas,[3] can all affect the location of targets and organs at risk (OARs). Farrugla et al. reported that there was considerable difficulty controlling tumor position in voluntary breath holds by 12.5% of patients.[3] Most patients spend their time in

the end exhale (EE) position and often conventional free-breathing treatments are planned in this phase,[4] and it is well known that it is a more reproducible technique for the treatment of upper abdominal cancers.[3] However, this technique has been found to be more challenging, and in need of more breaths when treating, than compared with end inhale, which is a more sustainable gating technique for patients.[5]

Stability and reproducibility of breath holds are paramount in treating pancreatic adenocarcinomas to obtain optimal target coverage while limiting dose to critical structures. The conventional treatment of pancreatic adenocarcinoma has many limitations due to the surrounding organs at risk and motion, with the biggest limiting factor being the duodenum. It has been previously reported by Taniguchi et al. that using the end expiration phase can result in a decrease in dose to the duodenum. This is because respiration causes the relationship to change between the duodenum and the pancreatic tumor. "The V20 to the duodenum averaged 5.9 cc when planned on end expiration and 7.2 cc when planned on end inspiration."[4] Little is known about how much other organs at risk are displaced or how much their volume has changed between these two techniques in the treatment of pancreatic cancer. It is standard to control breathing motion in the treatment of abdominal cancers using gating techniques with inspiration breath hold being the most common.

The traditional treatment regimen for treating pancreatic cancer is 45-50.4 Gray (Gy) in 25 to 30 fractions[6] using 3D-conventional or more commonly, intensity modulated radiation therapy (IMRT). IMRT has proven to be superior with the allowance of dose escalation through simultaneous integrated boosts. Dose escalation, along with chemotherapy has improved overall survival and locoregional control 3-fold.[6] Advancements in radiation treatment technology have now allowed pancreatic patients to be treated to higher doses in fewer fractions using stereotactic

body radiotherapy treatment (SBRT) technique[7]. A common dose fractionation schedule is 50 Gy in 5 fractions. Treating to these higher doses emphasizes the significance of protecting critical structures while still delivering accurate doses to the target, again stressing the importance of internal motion.[8]

One important limitation to using conventional linear accelerators is imaging. Even with advancements in technology, such as the use of cone beam computed tomography (CBCT), visualization of soft tissue is still difficult. This is due to increased noise level and poor soft-tissue contrast when compared to a diagnostic CT scan.[9] Fiducials in and/or around the target can help with visualization, as they can monitored with the use of image guided radiotherapy (IGRT)[2], but that leads to more imaging and increases dose to the patient. Tracking fiducials may aid in visualization of the location of the target but does not show other internal organ movement. MRI is the standard imaging modality for soft tissue imaging. Now through the use of MRI guided radiation therapy we can image while treating, without giving extra dose to the patient.[9]

Stereotactic MRI guided radiation therapy (SMART) is a relatively new treatment modality that can be used in the treatment of pancreatic adenocarcinoma.[10] It allows real time visualization of internal organ movement while treating simultaneously. The superior image quality allows for the use of online adaptive planning which aiding in the potential to dose escalate while still protecting normal tissue.[11] Adaptive therapy is not a new technique, it is often used when replanning for patient changes whether it is weight loss, set-up inaccuracies or target changes.[12] However, this process is usually done offline and does not take into account normal internal organ motion that occurs during that days treatment.[12] A entirely new plan is generated with offline adaptive planning and patients frequently have to go through the entire simulation process again, possibly delaying the patient's treatment.

To overcome these potential delays and internal daily changes, MRI-guided online adaptive radiotherapy allows the treatment plan to be adjusted while the patient is on the table. Studies have shown that day to day changes can vary as much as 2cm[13], this could be virtually unknown using CBCT only due to poor soft tissue visualization. Online adaptive planning uses the original treatment plan and the image taken from that day's treatment, generates a new plan that considers the intrafractional changes. Adaptive planning can often be lengthy so to help cut down on treatment planning time deformable registrations of contours in the ViewRay system are utilized. Also, the plans are reoptimized with the same parameters from the original plan.[13] The method allows for recontouring and generating new plans to give more accurate doses to targets and OARs. Adaptive replanning has shown to improve tumor coverage while decreasing dose to the duodenum.[14] Another advantage to online adaptive treatment is that air in the gastrointestinal can be accounted for and is beneficial as air in the stomach greatly affects dose to the PTV and surrounding organs.[14,15] Both the ViewRay MRIdian and the Elekta MRI-linac are able to employ online adaptive planning with real-time tracking and gating functionality.[13]

Even with these advancements it is still unknown what occurs to target, OAR volumes and doses between end inhale vs end exhale treatments. The goal of this study is to determine one technique is more optimal than the other, DI or EE, in the treatment of locally advanced pancreatic adenocarcinoma using the ViewRay MRIdian treatment planning system. The null hypothesis is that they are the same with the alternative hypothesis being that they are not the same. If they are not the same it will lead to more investigation.

Methods

Patient Selection

This retrospective dosimetric analysis included five patients with locally advanced pancreatic cancer that had previously been treated with MRI guided SBRT. The subjects were anonymized and therefore no identifiable background information is known. The inclusion criteria were patients that had previously been treated using a deep inspiration breathhold (DIBH) gating technique and treated on the ViewRay MRIdian Linac^{TM} (ViewRay, Inc., Oakwood Village, Ohio, USA).

Simulation

Each patient was simulated using a GE lightspeed 16RT computed tomography (CT) scanner. Prior to their appointment they were instructed to not have anything to eat or drink four hours prior to their procedure (NPO). They were in the supine position with arms by their side, centered on the simulation table with MRI coils underneath and above them. A 3D simulation was obtained while the patient was instructed to hold their normal inhale breath. Patients were coached to not hold their deepest breath to enhance reproducibility. The CT simulation scans were not used for planning purposes. They were used to confirm isocenter placement and to obtain the correct Hounsfield units for dosimetric purposes. Once the CT was obtained the patients were marked at the isocenter that the MD selected. They were then given 8 ounces of water to drink, to aid in visualization of the duodenum on the MRI, and transferred over to the MRI linac for the next portion of the simulation.

During the MRI simulation the patients were set-up in the same position as on the CT table. Two MRIs to be used for treatment planning were obtained. One with the same inspiration breath as was instructed during the CT (MR_D) and one while the patient was holding the exhale portion of their breathing cycle (MR_{EE}). The patients were treated using the inspiration technique due to

physician choice. After the simulation scans were complete patients were given tattoos for aid in reproducing the setup when treated.

IRB

A Data Review Protocol was submitted to Dartmouth Health and found to be exempt. The protocol outlined the background, endpoints and methods for the study. Also, any potential risks and how they were mitigated relating to the privacy and protection of patient's and patient information. The patients in this study were anonymized by the primary invistigator and all identifying information was restricted on a password protected internal system. There were no medical risks for the participation subjects and there was a minimal risk of loss of confidentiality should access be gained to the password protected data linking the anonymized identification to patient medical record numbers. The study was also submitted the Grand Valley State University (GVSU) Institutional Review Board (IRB) and approved under the exempt review category.

Planning

For this retrospective analysis the original planning computed tomography (CT) and ViewRay MRI, DI and EE, scans were anonymized, registered, and imported into the ViewRay treatment planning system (VR-TPS), for a total of ten treatment plans. The planning and contouring parameters that were followed were from ViewRays SMART trial protocol for the treatment of LAPC (VR C2T2 – SMART- LAPC/BRPC 1). [16] The same physician and resident contoured the targets and relevant organs at risk (OARs) on the MRI images. The gross tumor volume (GTV) was contoured and then expanded to include the superior mesenteric vessel and celiac axis nodes (CTV). Then a planning target volume (PTV) was created to encompass the CTV

with a 3mm expansion. The OARs included the small bowel, large bowel, duodenum and stomach. They were contoured on all slices 3cm superior and inferior to the PTV.

The plans were completed by the same two dosimetrists to ensure the same process was used for all patients. The dosimetrists reviewed the given contours and created the necessary planning structures. Rules were created and used in the treatment planning system to create the following optimization structures and were exactly the same for all patients. The first structure was a PTV optimization structure (PTV_OPT) which is done by subtracting the PTV from any overlying OARs. Next a ring was created around the PTV by expanding the PTV volume 3cm in the sagittal and coronal direction and 1.5 cm in the axial (zPTV_PRV30). Then the OARs within this volume were booleaned together (zOARs_3). An optimization structure was created to give 0.3cm of fall off between the PTV and zOARs_3 (zOptPTV High) as the OARs were the limiting dose factor. Then dose rings were created, an inner ring (zInner) by expanding the PTV by 3mm and subtracting it from the zPTV_PRV30 and a mid ring (zMid), a 3cm expansion on zPTV_PRV30 and then subtract zPTV_PRV30. If the zMid expands outside the body it was cropped to be within the skin structure. See figure 1 in the appendix.

Once all planning structures were created the next step of the process was to confirm the fusion from the imported CT scan and confirm the correct isocenter. Then in the beams section of the TPS beams were placed. The goal was to use as many beams as possible without any directly opposing one another. A range from 19-21 beams was used. Beams that traveled through the patient's arms or the beveled edge of the treatment table were removed. The prescription dose was confirmed as well as the default electron density table: 22.5 mm. The table factor was selected as the DHMC Scanner. Sequencing was set to 40 segments and Bixels set to an IMRT efficiency of 8. In the dose tab the magnetic field was set to yes and geometry to 0.2cm.

Next, objectives and constraints were created. A max constraint of 32 Gy was added to the zOARs_3, 1 Gy under the prescription max of 33 Gy. A max dose constraint of 65 Gy was also added to the PTV, this is 130% of the PTV. In the SMART trial protocol, which was used as a guideline when treating pancreas patients, the max dose to the PTV is 140%. These two constraints were activated and then the objectives are created. The goal was to maximize dose to the PTV without going over the dose limits to the OARs and to limit 50% of the dose outside of the zPTV_PRV30. The zOptPTV_High, zInner, zMid and skin were used as starting objectives with specific priorities and thresholds, these had the ability be adjusted after the initial optimization. See figure 2 in the appendix. The plan was then optimized and coverage was assessed. If the nearest limiting OAR was not meeting the constraint of 0.5cc to 33Gy, each plan was dose escalated by normalizing the plan lower to meet the limit of the OAR. To maximize coverage to the target, without going over OAR constraints, the thresholds and powers of the objectives were also adjusted in the optimization process. This ensures the patient is receiving the highest dose to the tumor.

Results

The goal of this study was to determine if there was an optimal gating technique between deep inspiration breath hold and end expiration breath hold for online adaptive treatment planning for locally advanced pancreatic cancer. The CTV, stomach and duodenum were evaluated for dose coverage and volume changes for five previously treated patients. The duodenum and the stomach were especially important organs at risk as they were the most common dose limiting structures.

CTV

According to the SMART Trial protocol, the target dose to the CTV is 100% of the volume to receive 95% of the prescription dose, or 47.5Gy.[16] This coverage was assessed for both the DI and EE plans. A nonparametric sign test was performed, and there was no statistically significant difference in the coverage of the CTV by the 95% isodose line in the DI CTV volume (M=95.396, SD = 3.59) and EE CTV volume (M = 91.698, SD = 6.896) $p = 0.125$. See figure 3 and table 3 in the appendix. Only two patients were able to achieve the CTV coverage objective for both the deep inspiration and end exhale scans, patients two and three. Due to the limited number of patients and the possibility of one number skewing the data, each patient was evaluated individually. Greater than 90% of the CTV volume was covered by the 95% isodose line in patients one, two and three for the DI and EE plans. For the DI plans, the CTV volume covered by the 95% isodose line was 94.69%, 100% and 97.88% and 92.29%, 100%, and 96.55% respectively. Patients four and five had the worst coverage on both plans, 90.91% and 93.5% for DI and 86.04% and 83.61% for EE. See table 1 in the appendix. The SMART Trial protocol allows for the CTV dose to fall within the range of 60-90% of the volume receiving 95% of the prescription dose. The minimum volume coverage of the CTV at 95% of the prescription dose was acceptable at 90.91% for the DI and 83.61% for EE plans, see Table 2 descriptive statistics in the appendix.

Duodenum

According to the SMART trial protocol, the dose to the OARs are not to exceed 33 Gy to 0.5 cc of the organ.[16] Due to the nature of planning on the ViewRay, the entire organs at risk were not contoured beyond five centimeters from the PTV. The treatment planning goal was to keep the 33 Gy isodose line within a three-centimeter ring around the PTV (zPTV_PRV_30), therefore only the volume of the duodenum that lies within the 3 cm ring was evaluated in all the plans. The amount of duodenum within the zPTV_PRV_30 was not found to be a statistically significant

difference for the DI plan (M=53.492, SD = 28.494) or the EE plan (M=58.752, SD = 30.859) p = .375. See figure 4 and tables 2 and 3 in the appendix. Again, due to the sample size the patients were evaluated individually. Only one patient, patient one, had a decrease in volume of the duodenum from the DI to the EE plan, in which the volume of the duodenum decreased from 74.2cc to 67.51cc. In patients two through five, the volume of the duodenum increased from the DI to the EE plans, 18.45cc to 20.67cc, 36.41cc to 38.51cc, 48.94cc to 65.59cc and 88.94cc to 101.48cc respectively. See table 1 in the appendix.

In five out of the ten total plans it was the duodenum that determined the normalization of the plans. Patient's one, four, and the EE of patient five were normalized down so that the duodenum met the maximum dose constraint, 33 Gy to 0.5cc. For patient two the duodenum in the DI plan received 33 Gy to 0.26cc and 0.18cc on the EE plan. With patient three the duodenum received 0.39 cc to 33 Gy on the DI plan and 0.43 cc on the EE. Oddly, the DI plan on patient five was normalized to the small bowel and the volume of the duodenum the received 33 Gy was 0.47cc. See table 1 in the appendix. The volume of small bowel that received 33 Gy on the exhale scan was 0.06cc. There was no significant data between the DI (M=.424, SD=.102) and EE plans (M = .422, SD = .139) p = 1.000 for the volume receiving 33 Gy. See figure 5 and tables 2 and 3 in the appendix.

Stomach

There was no statistical significance in the change of volume of the stomach between the DI (M = 53.094, SD =23.502) to the EE (M = 46.556, SD = 19.2698) p = 0.375. See figure 6 and tables 2 and 3 in the appendix. The volume of the stomach within the zPTV_PRV30 decreased from the DI to the EE plans in four out of five patients. Patient five had the biggest difference in volume from the DI 77.79cc to 56.63cc in the EE plan. Patients one, two and three decreased from

65.5cc, 63.8cc, 19.49cc for the DI plans to 60.91cc, 60.0cc and 15.79cc for the EE plans. Patient four had a slight increase from DI 38.89cc to EE 39.45cc. See table 1 in the appendix.

There was also no significance found between the DI (M = .306, SD = .185) and EE (M = .232, SD = .250) plans for the volume that received 33 Gy, p = .250. See figure 7 and tables 2 and 3 in the appendix. Four out of the ten plans were normalized to the stomach with the same absolute volume-based constraint of 33 Gy to 0.5cc. This occurred in patients two and three. The volume receiving 33 Gy in patients one, four and five was 0.2cc, 0.24cc and 0.09cc for the DI plans and 0.14cc, 0.02cc and 0cc for the EE plans. See table 1 in the appendix.

Discussion

The purpose of this study was to determine if there was a more optimal gating technique, deep inspiration versus end exhale, in the treatment of locally advanced pancreatic adenocarcinoma, regarding target coverage and the sparing of organs at risk using the ViewRay MRIdian Linac. The challenge in treating this area with radiation is due to target and OAR motion from breathing, peristalsis, and the movement of bowel gasses.[3] Previous literature has shown that patients spend more time in the end exhale phase of breathing and conventional free breathing treatments are planned in this phase.[4] For patients that are treated using a gating technique, deep inspiration breath hold is the most common due to it being more sustainable for patients.[5] With the advancement of technology and employment of the ViewRay MRIdian, online adaptive planning with real time imaging and tracking can be used in the treatment of LAPC.[10] This treatment technique has shown to improve target coverage while decreasing dose to the OARs.[14] An optimal gating technique has yet to be discovered.

CTV

Though there was no significant data supporting a gating technique, there were some trends that were observed. CTV coverage was worse in four out the five exhale plans compared to the deep inspiration plans at the prescription target coverage of 95% of the dose to 100% of the target volume. Only two patients were able to meet the objective. However, the SMART trial protocol that was used for treating these plans states that because the OARs are the limiting dose factor the volume of the CTV that receives 95% of the prescription dose often falls between 60-90%. If this was taken into consideration then all ten plans were acceptable in the protocol standards.[16] All five inhale plans also showed over 90% coverage. Patient's four and five showed the largest difference in coverage from the inhale to the exhale plans. The limiting factor for coverage of the target greatly depended on the normalization of the OAR structures. For this group of patients, the most common was the duodenum and the stomach.

Duodenum

The sample size being small aided in the lack of statistical significance and increased the importance of finding trends between the individual patients became valuable. The duodenum is the closest OAR to the pancreatic head and was found to be the dose limiting structure in five out of the ten treatment plans. Patient's one, four and five were all normalized to the duodenum limit of 0.5 cc to 33 Gy in three exhale and two inhale plans. The volume of the duodenum that fell within the zPTV_PRV30 in all the plans was the largest in all three of these patients. Possibly leading to why it was the most common dose limiting structure, location and size. The only difference was the inhale plan on patient five was normalized to the small bowel. However, the duodenum was almost at its constraint with 0.47 cc receiving 33 Gy. Patient five also had the greatest difference in the volume of the duodenum, 88.94 cc in the DI plan and 101.48 cc in the exhale plan. With the patient being NPO for four hours prior to their simulation it can possibly be

assumed that the difference in the size of the duodenum was due to the different breathholds and not because of other factors, such as peristalsis. However, the 8 ounces of water introduces some bias. The slight trend that the duodenum was the dose limiting structure in three of the exhale plans did not follow previous literature.

It had been previously reported that the dose to the duodenum was higher in patients that used a deep inspiration breath hold technique.[4] The hypothesis our study group had was the potential for the compression of the organs in the DI breath hold would lead to more of the OARs being exposed to higher doses. The volume of the duodenum that received 33 Gy from the exhale to the inhale plans showed a decrease in four out of five patients, which does not support the previous theory. Three of the five patients were normalized to the duodenum in the EE plans compared to only two for the inhale plans. The patients that were normalized to the stomach had the smallest duodenal volume in all the plans.

Stomach

The stomach was the other most common limiting OAR structure. It was normalized in both the DI and EE plans for patients two and three. Aside from patients two and three, the volume of the stomach that received 33 Gy was marginally larger in all three remaining patients for the DI plans. The volume of the stomach within the zPTV_PRV30 was larger in four out five patients, possibly aiding to why a larger volume received 33 Gy. However, patient four had a marginal decrease in volume within the zPTV_PRV30 from the EE to DI of 0.56cc. This did not aid in any statistical significance.

Limitations and Future Research

The major limitation in this study was the sample size. Only five patients were assessed and without any major deviations there was no statistically significant data. There was also no way to gauge how a patient was holding their breath. Breath holds are rarely consistent,[3] and it is unclear what the instructions were for breath holding, whether or not to use a belly or a chest breath. There were also a lot of variables that could have been used for evaluation with such a small sample size finding the correct ones were extremely difficult. Other variables that could have influenced the target coverage were also not evaluated, such as air near the target or if the 8 ounces of water was affecting volume due to peristalsis. With further research and a larger sample size it may be possible that an optimal gating technique could be found.

One possible further addition to this study would be to do a prospective study on an end-exhale plan and a free breathing treatment. Studies have shown that most patients spend their time in an exhale phase in a normal breathing pattern and that it is more reproducible than DI. With real time tracking the technique could possibly be used in the advancement of treating locally advanced pancreatic cancer. This could lead to shorter treatment times and be more comfortable for the patient. Another aid to shorter treatment times and patients hitting their breathing targets is the use of visual gating aids where patients are able to see their breathing target and adjust their breath to reach that target, making them more in control of their treatment.

Conclusion

Locally advanced pancreatic cancer is an aggressive cancer with a dismal outlook. The only chance for a cure is surgical resection.[1] Due to the limited amount of patients that are candidates for surgical resection, radiation is often used as a common treatment modality.[2] Radiation is still limited because of high gastrointestinal (GI) toxicity because of the adjacent

organs at risk that are so near to the pancreas.[8] Another challenge for radiation treatment is the motion from breathing and other involuntary motions such as peristalsis and the motion of gas through the GI system.[3] To overcome some of these limitations institutions often use a gating technique during radiation treatment.

There was no statistically significant data for this study regarding CTV coverage and the sparing of OARs between the DI and EE plans. Coverage was acceptable in all the plans according to the SMART trial protocol. The stomach and the duodenum were the most common limiting structures. Further evaluation is needed to determine if there is an optimal gating technique.

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Appendix

Table 1.

Patient	Inhale_CTV	Exhale_CTV	Inhale_DuodenumV33	Exhale_DuodenumV33	Inhale_StomachV33	Exhale_StomachV33	Inhale_DudenumV3	Exhale_DuodenumV3	Inhale_StomachV3	Exhale_StomachV3
1	94.69	92.29	0.5	0.5	0.2	0.14	74.72	67.51	65.5	60.91
2	100	100	0.26	0.18	0.5	0.5	18.45	20.67	63.8	60
3	97.88	96.55	0.39	0.43	0.5	0.5	36.41	38.51	19.49	15.79
4	90.91	86.04	0.5	0.5	0.24	0.02	48.94	65.59	38.89	39.45
5	93.5	83.61	0.47	0.5	0.09	0	88.94	101.48	77.79	56.63

Table 2.

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Inhale_CTV	5	95.3960	3.59112	90.91	100.00	92.2050	94.6900	98.9400
Inhale_DuodenumV33	5	.4240	.10213	.26	.50	.3250	.4700	.5000
Inhale_StomachV33	5	.3060	.18542	.09	.50	.1450	.2400	.5000
Inhale_DudenumV3	5	53.4920	28.49406	18.45	88.94	27.4300	48.9400	81.8300
Inhale_StomachV3	5	53.0940	23.50214	19.49	77.79	29.1900	63.8000	71.6450
Exhale_CTV	5	91.6980	6.89645	83.61	100.00	84.8250	92.2900	98.2750
Exhale_DuodenumV33	5	.4220	.13864	.18	.50	.3050	.5000	.5000
Exhale_StomachV33	5	.2320	.25044	.00	.50	.0100	.1400	.5000
Exhale_DuodenumV3	5	58.7520	30.85903	20.67	101.48	29.5900	65.5900	84.4950
Exhale_StomachV3	5	46.5560	19.26983	15.79	60.91	27.6200	56.6300	60.4550

Table 3.

Test Statistics[a]

	Exhale_CTV - Inhale_CTV	Exhale_DuodenumV33 - Inhale_DuodenumV33	Exhale_StomachV33 - Inhale_StomachV33	Exhale_DuodenumV3 - Inhale_DudenumV3	Exhale_StomachV3 - Inhale_StomachV3
Exact Sig. (2-tailed)	.125[b]	1.000[b]	.250[b]	.375[b]	.375[b]

a. Sign Test

b. Binomial distribution used.

Figure 1. Ring creation

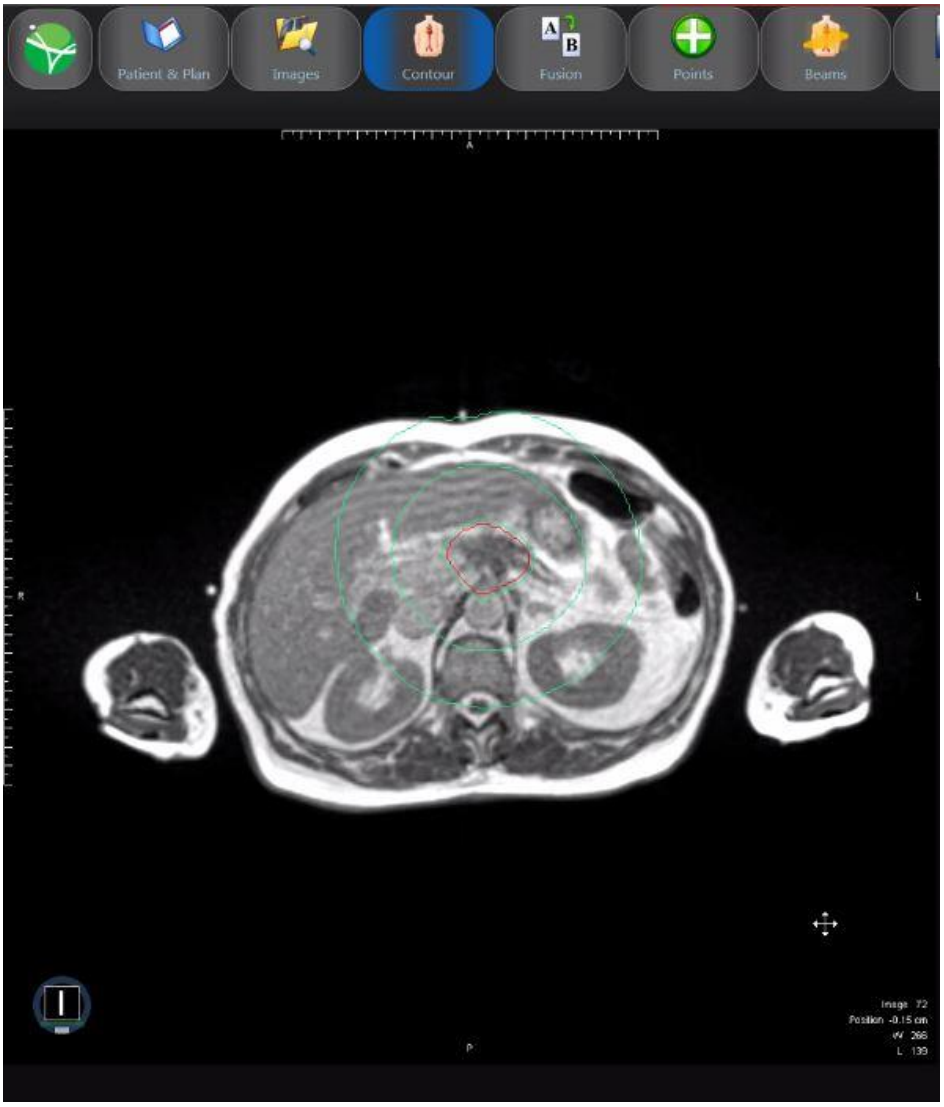

Figure 2. Objectives starting point

zPTVopt_High	Increase Dose	5	5	50	Gy
zRing_Inner	Decrease Dose	3	3	49	Gy
zRing_Mid	Decrease Dose	3	3	20	Gy
Skin	Decrease Dose	4	4	8	Gy

Figure 3. Mean CTV coverage of the 95% isodose line

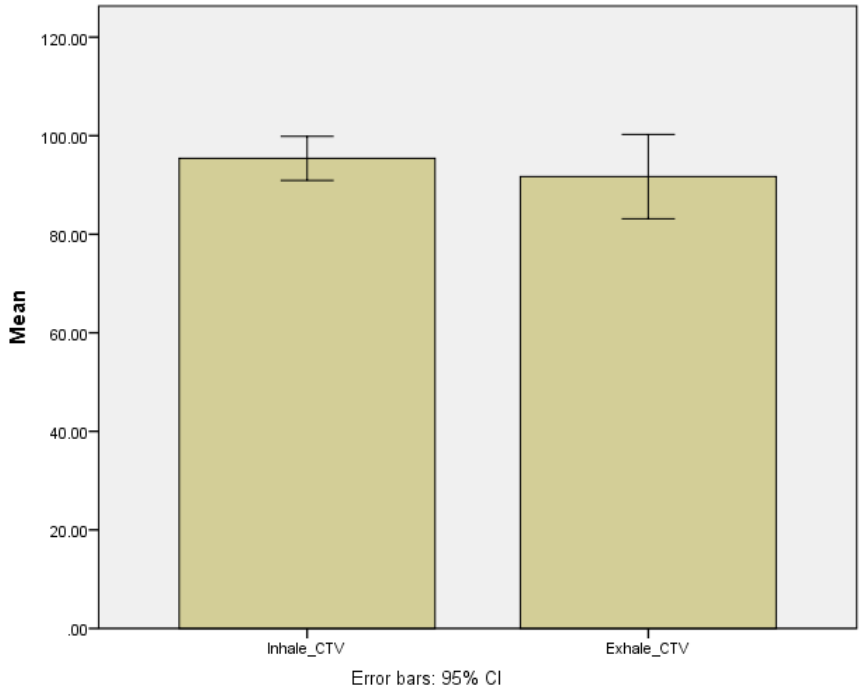

Figure 4. Mean duodenal volume within zPTV_PRV_30

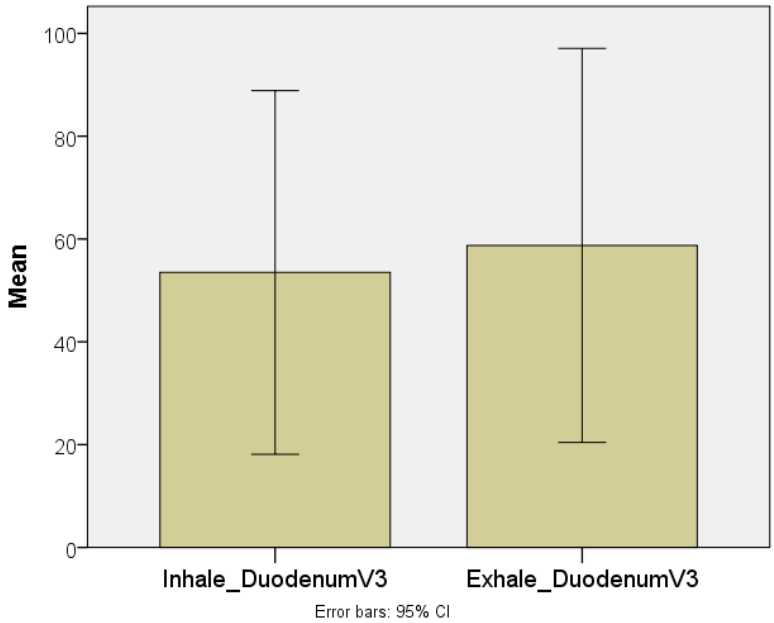

Figure 5. Mean duodenal volume receiving 33 Gy within zPTV_PRV_30

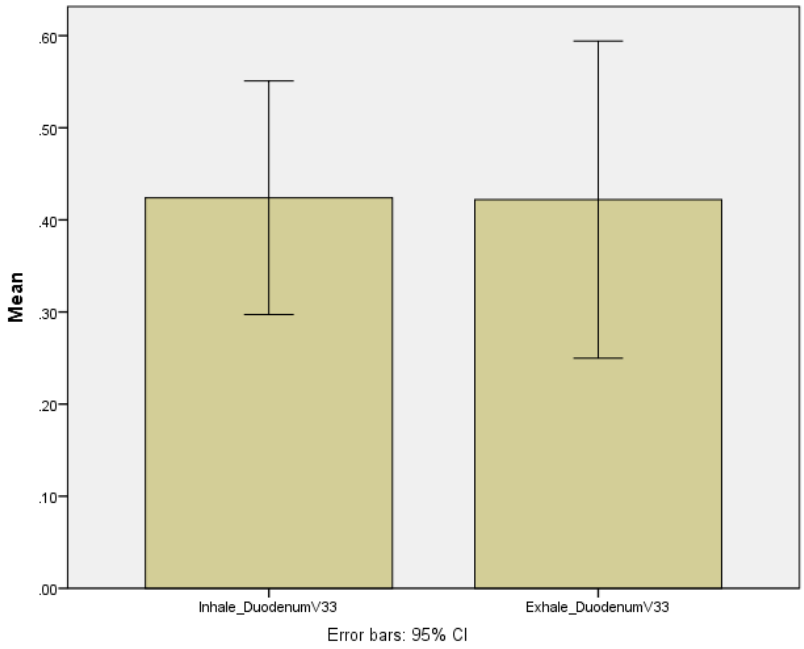

Figure 6. Mean stomach volume within zPTV_PRV_30

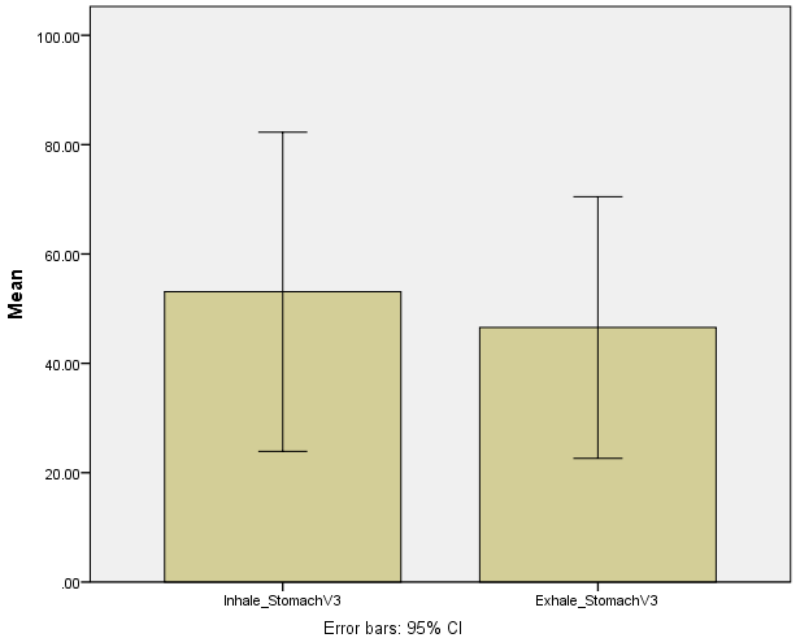

Figure 7. Mean stomach volume receiving 33 Gy within zPTV_PRV_30