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Analysis of PTV Margins for VMAT Treatment of Rectal Cancers Utilizing Prone Bellyboard Device.

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Abstract

Introduction

Utilization of a bellyboard device reduces small bowel dose for patients receiving radiation therapy for rectal cancer. The reduction of small bowel dose with the bellyboard is even more significant in intensity modulated radiation therapy rectal treatments, as opposed to conventional 3D treatments. However, there is evidence of increased setup variation with prone bellyboard positioning, especially in pitch and roll. The purpose of this study is to determine the margin needed between the clinical target volume and the planning target volume to adequately account for these setup variations when planning volumetric modulated arc therapy rectal cases utilizing the bellyboard device. The most preferable margin will provide the highest clinical target volume (CTV) dose coverage without significantly increasing normal tissue dose, as assessed through on-treatment cone beam computed tomography imaging.

Methods

This study utilized retrospective data from seven rectal cancer patients that received radiotherapy treatment prone on a bellyboard device at a pair of Midwest Hospitals. Using computed tomography simulation data, three volumetric modulated arc therapy (VMAT) plans were created for each patient. The three treatment plans differ in the amount of margin added to the CTV to create the planning target volume (PTV). A 0.5cm margin was used in the superior-inferior direction and the anterior-posterior margin will vary between the three plans (0.5, 0.8, and 1.0 cm). Varian Eclipse image registration software was used to calculate the dose a patient would have received based on cone beam computed tomography imaging. The appropriate CTV-to-PTV margin was determined by comparing the dose delivered to the CTV and normal structures.

Results

Variations in pitch were a significant predictor of differences in CTV coverage between the three plans ($p < .0001$, $\chi^2 = 55.5$). Between the 0.5 cm and 0.8 cm plans: CTV 98% increased by 0.97% (95% CI 0.73-1.22%, $p < .0001$). Bowel V45Gy increased by 4.82 cc (95% CI 3.13-6.52 cc, $p < .0001$). Bladder V40Gy increased by 4.79 cc (95% CI 3.55-6.03 cc, $p < .0001$). Between the 0.5 cm and 1.0 cm plans: CTV 98% increased by 1.41% (95% CI 1.04-1.77%, $p < .0001$). Bowel V45Gy increased by 8.91 cc (95% CI 5.25-12.56 cc, $p < .0001$). Bladder V40Gy increased by 9.90 cc (95% CI 7.54-12.27 cc, $p < .0001$).

Conclusion

Utilization of a 1.0 cm axial margin leads to a significant increase in CTV coverage by 98% of the prescription dose. Corresponding increases in OAR doses are still within generally accepted tolerances and can be mitigated through proper use of bellyboard positioning, bladder filling and VMAT techniques.

Introduction

Colorectal cancer is the third-most prevalent cancer diagnosis in both men and women, following breast, prostate and lung cancer. There were an estimated 101,420 new cases of colorectal cancer in 2019. An estimated 44,180 of these individuals were diagnosed with rectal cancer. Colorectal cancer is the third leading cause of cancer death for both men and women, accounting for an estimated 51,020 deaths in 2019[1]. Rectal cancers most commonly present as stage 2-3 and 5-year overall survival for these patients is approximately 65%[2]. Locally advanced rectal cancer is treated using a multimodality approach of neoadjuvant chemoradiation, followed by surgical resection and adjuvant chemotherapy.

The rectum is located at the end of the gastrointestinal tract, just proximal to the anal canal. The rectum begins anterior to the sacrum around the 3rd sacral segment, and follows the curvature of the sacrum. The rectum is typically 4 to 5 inches in length. The upper third of the rectum and the anterior wall of the middle third is covered by serosa, while the lower third is covered only by a muscularis layer. The peritoneal reflection is the point where the serosa reflects superiorly to cover the upper portion of the rectum. First station lymphatic drainage for the rectum includes the internal iliac and presacral lymph nodes, followed by the common and paraaortic nodes[3].

Rectal cancer is associated with a diet high in fat and red meat and low in fiber. Presenting symptoms often include rectal bleeding or changes in bowel habits. The most common histological subtype in rectal cancer is adenocarcinoma. Patterns of failure in rectal cancer are often determined by their location relative to the peritoneal reflection. Tumors located above the peritoneal reflection have an increased likelihood of distant failure. These tumors have the ability to penetrate the peritoneum and seed into the abdominal cavity. Local recurrence is the most common method of failure for tumors located below the peritoneal reflection. Without an outer

serosal layer, these lesions are much more likely to directly invade or adhere to adjacent organs in the pelvis[4].

Surgical resection with total mesorectal excision is the primary treatment for cancers of the rectum. This technique involves removal of an intact portion of the rectum along with surrounding mesorectal fatty lymphovascular tissue. Excision of the entire mesorectal envelope results in lower postoperative morbidity and local recurrence, while improving long-term survival. There are two main surgical approaches depending on the location of the primary tumor within the rectum. If the tumor is located higher in the rectum an anterior resection or a low anterior resection (LAR) may be performed with a colo-anal anastomosis to salvage some normal bowel function. A tumor located closer to the anus would necessitate an abdominoperineal resection (APR), in which the affected area of the rectum and the anus are removed, leaving the individual with a permanent end colostomy[5].

The National Comprehensive Cancer Network recommends combined modality treatment for T3 or T4 rectal cancer, as well as node-positive disease[6]. A multi-modality approach has been shown to reduce the risk of local recurrence and the morbidity associated with salvage therapy after local recurrence. This regimen consists of neo-adjuvant radiation therapy with concurrent chemotherapy, followed by surgery 6-8 weeks later with further adjuvant chemotherapy. Fluorouracil (5-FU) is the primary neo-adjuvant chemotherapy agent, a radiosensitizer used to enhance the effects of radiation treatment. Newer chemotherapy regimens have replaced 5-FU with oral capecitabine with the aim of reducing small bowel toxicities. The most commonly used fractionation scheme in the United States consists of 45 Gy to the clinical target volume with a 5.4 Gy boost to the primary tumor and involved lymph nodes in 28 daily fractions[7].

In 2010 Radiation Therapy Oncology Group (RTOG) established consensus guidelines for the delineation elective clinical target volumes (CTV) to be used for planning pelvic intensity-modulated radiotherapy (IMRT) for rectal cancers. For the majority of locally advanced rectal cancers the CTV consists of the internal iliac, pre-sacral and peri-rectal nodal groups. The CTV should extend no less than 2 cm below any gross disease or to the pelvic floor, whichever is lower. In the mid-pelvis, the CTV should extend to the pelvis sidewall musculature posterior and laterally. The anterior margin should include 1 cm of the posterior bladder, to account for day-to-day variation in bladder position. The upper margin of the CTV should be where the common iliac vessels bifurcate into external/internal iliacs (approximately at the level of the sacral promontory), in order to ensure proper coverage of the internal iliac and pre-sacral nodal regions. The CTV should extend posteriorly to within 1 cm of the sacrum to provide proper coverage of the pre-sacral region[8].

Organs at risk during radiation therapy for rectal cancer include the bladder, femoral heads and the small bowel. Acute diarrhea is the most common side-effect of pelvic irradiation, and it is often compounded by the concurrent chemotherapy regimens used for rectal cancer. Grade 3 acute diarrhea can lead to failure to complete therapy and may be associated with the development of chronic diarrhea. The connection between high radiation doses (>45 Gy) and small bowel toxicities is well established, and more recent studies have also shown a link between the volume of small bowel receiving doses as low as 15 Gy and Grade 3 toxicities[9].

In order to minimize small bowel dose, it is important to move the small bowel out of the treatment fields as much as possible. A simple and effective means of accomplishing this is through prone patient positioning and the use of a bellyboard device. Small bowel is displaced anteriorly and superiorly by allowing the patient's abdomen to protrude through a cutout in the

device. Use of prone positioning with the bellyboard device in combination with a full bladder has been shown to reduce the volume of small bowel in the treatment fields by 70%[10]. However, there is evidence that use of the bellyboard device results in decreased reproducibility of patient setup, especially in pitch and roll[11]. These variations need to be accounted for when considering the use of highly conformal radiotherapy techniques such as IMRT or volumetric modulated arc therapy (VMAT).

The utilization of IMRT as an alternative to 3D-conformal radiation therapy (3DCRT) has significantly increased over recent years[12]. Historically, the standard was to use a 3-field technique, consisting of two wedged laterals and a posterior-anterior field. This method provides excellent target coverage and well-tolerated toxicities. However, the current focus on intensification of neo-adjuvant chemotherapy and the addition of novel radiosensitizers, has contributed to the desire to lower radiation induced toxicity rates even further[13].

Both IMRT and VMAT techniques have the ability to achieve higher tumor doses while sparing more normal tissue. By reducing the volume of small bowel irradiated, these techniques have the potential to decrease gastrointestinal (GI) toxicities in the treatment of locally advanced rectal cancers. In several retrospective dosimetric comparison studies between IMRT and 3DCRT, small bowel sparing was significantly improved while target coverage and conformity was maintained. The volume of small bowel receiving 15 Gy was also reduced with IMRT treatment[14-17].

Despite dosimetric advantages, there is conflicting evidence whether IMRT provides any clinical benefit to GI toxicity. Several retrospective studies have shown IMRT to reduce GI toxicities and diarrhea when compared to 3DCRT[18-20]. A pair of RTOG trials were used to compare the GI toxicity rates between patients treated with IMRT vs 3DCRT neo-adjuvant

radiation with concurrent capecitabine/oxaliplatin for locally advanced rectal cancer. IMRT was unable to reduce the high rates of GI toxicity or diarrhea that are associated with oxaliplatin[21]. Furthermore, a nationwide retrospective analysis conducting using data from the National Cancer Database determined that IMRT did not improve perioperative outcomes or overall survival[12].

Studies comparing VMAT treatment to 3DCRT have been more limited. In two retrospective dosimetric studies the small bowel V15 was significantly lower for VMAT vs 3DCRT[14,17]. In another study, the small bowel V40 was reduced by 60% for patients receiving VMAT[15]. The only study comparing GI toxicity between VMAT and 3DCRT reported a 41% downstaging rate with IMRT and comparable toxicity rates between the two groups[22].

With the increasing use of IMRT techniques to treat locally advanced rectal cancer, the continued use of the bellyboard device has come into question. Recent research has shown that IMRT used in conjunction with the bellyboard device is the most effective means of reducing small bowel dose[23]. The study's author posits that similar results would have been found if they had utilized VMAT.

When highly conformal treatment techniques such as VMAT are used, any discrepancies in day-to-day patient setup can greatly affect dosimetric target coverage. The variations created by use of the bellyboard device need to be adequately accounted for during the planning process.

ICRU Report 83 states that the purpose of the PTV is "…to ensure that the prescribed absorbed dose will actually be delivered to all parts of the CTV with a clinically acceptable probability, despite geometrical uncertainties such as organ motion and setup variations." The report also reiterates the need for PTVs to be customized based on individual cancer sites, treatment techniques, and patient positioning factors[24]. The problem of determining appropriate CTV to planning target volume margins has been investigated by various researchers.

Mathematical formulas have been developed to estimate the necessary CTV-PTV margin based on observed systematic and random errors[25]. Post-treatment cone beam computed tomography (CBCT) images have been used to determine the degree of geometric miss when using standard CTV-to-PTV margins[26]. Off-line image registration of cone beam computed tomography scans and planning computed tomography (CT) scans have also been used to determine setup variability and calculate appropriate margins[27].

The purpose of this study is to determine the appropriate CTV-PTV margin needed to account for the variation in patient setup using the bellyboard device. Multiple VMAT plans will be created to determine if varying the CTV-PTV margin has a significant effect on the total dose delivered to the CTV over the course of treatment based on setup variations observed on CBCTs. If any margin significantly improves the CTV dose coverage, further analysis will be performed to determine the most optimal margin. Any change in small bowel dose between the margins will have to be weighed against the perceived clinical significance of the increased dose to the CTV.

Methodology

Patient Selection

This study is a retrospective dosimetric analysis of 7 patients with locally advanced rectal cancer that had been previously treated with radiation therapy utilizing the bellyboard device. The subjects were treated at a pair of Midwest Hospitals and their data was obtained via a shared electronic medical record system. All of the subjects were originally treated with a traditional 3-field wedged pelvis technique while positioned prone on a bellyboard device. In order to be included in the study, subjects needed to be over 18 years of age, diagnosed with locally advanced

rectal cancer and previously received radiation therapy whilst positioned prone on a bellyboard device.

Most often 3D-conformal rectal treatments use on-board planar imaging to confirm patient positioning, mainly relegating CBCTs to the assessment of bladder filling. As such, the number of study participants was limited by the availability of subjects who fit the criteria and also had a sufficient number of pre-treatment CBCTs available to represent patient positioning throughout the course of treatment. For each subject in the study, the number of available CBCTs varied from 5 to 20. To homogenize the data, six CBCTs were utilized for each patient, with the exception of one subject who only had five available. The six CBCTs were randomly selected from the total available for each subject. If a subject had multiple CBCTs from a given treatment day, only the final pre-treatment CBCT was considered for use in the study.

Institutional Review Board

The study was approved by the institutional review boards (IRB) of both Midwest Hospitals from which patient data was obtained and by the Grand Valley State University IRB. Informed consent was waived by the review boards due to the retrospective nature of the study and the minimal risks to patient privacy. The IRB protocols outline the measures taken to safeguard patient privacy in accordance with the Health Insurance Portability and Accountability Act of 1996.

The Varian Eclipse treatment planning system (TPS) was used to strip data sets of any protected health information and export them to an external system folder on the hospital shared drive. The anonymized copies of subjects' CT simulation and CBCT data sets were then imported back into Eclipse and stored in the electronic medical records of temporary "anonymous" patients. The external folder was deleted after all data sets were imported. All "anonymous" patient records, and data sets contained therein, were erased at the conclusion of the study.

Simulation

Simulation protocol was similar at both Midwest Hospitals. Each patient underwent a CT simulation in the prone position on the CIVCO carbon fiber bellyboard device (Figure 1). The subjects were marked with three tattoos to aid in setup, two lateral marks and one posterior mark. A scale on the side of the CIVCO bellyboard allows for reproducible positioning of the patient relative to the device. Depending on physician preference, some patients were administered oral contrast in order to better visualize the small bowel and rectum on the planning CT. One site used a Siemens SOMATOM CT scanner and the other utilized a Philips Big Bore CT scanner.

Planning

All of the patients involved in this study originally received external beam irradiation using a 3D-conformal technique consisting of one posterior-anterior field and two wedged laterals. When using 3D-conformal techniques, it is not necessary to contour nodes to be included in a clinical target volume (CTV), because field margins are determined by bony landmarks. However, as this study seeks to evaluate target margins for VMAT techniques, it was necessary to create CTVs for each of the subjects. The CTVs were contoured in accordance with the RTOG consensus guidelines mentioned previously[8]. The principle investigator created the CTV contours and they were approved by a board-certified radiation oncologist.

Contouring and planning was done using the Varian Eclipse TPS (v.15.6). Bladder and small bowel were contoured in order to provide dose information on these critical structures. On the CT simulation images, each loop of small bowel was contoured individually, with oral contrast (if present) contoured and assigned the density of air.

The standard for VMAT rectal cases is a symmetrical 0.5 cm CTV-PTV margin[21]. Since pitch and roll are the major causes of setup discrepancy when using the bellyboard[11], the margins utilized in the comparison plans differ only in the radial dimensions. Three plans were created for

each patient. The first plan had symmetrical 0.5 cm CTV-PTV margins. The second had 0.8 cm margins radially and 0.5 cm margins craniocaudally. The third plan had 1.0 cm margins radially and 0.5 cm margins craniocaudally (Figure 2).

VMAT plans with two partial, posterior arcs were used to reduce small bowel and bladder dose. All plans were required to meet the coverage guidelines established in RTOG 0822[21]. Coverage of >98% of the PTV with 95% of the prescribed dose, with <10% receiving 105% and <5% receiving 110% of the prescribed dose. Small bowel dose was limited to V35 <180 cc, V40 <100 cc, and V45 <65 cc. Bladder dose was limited to V40 <40%, V45 <15%, and a maximum dose 50 Gy.

The same planner created each plan in the study to exclude any confounding variance introduced by planner specific skill or technique. The nature of the VMAT optimization process makes the creation of identical plans with different PTVs impossible, but measures were taken to ensure adequate similarity for the sake of comparison. After the baseline 0.5 cm CTV-PTV margin plan was created for each patient, optimization objectives were altered as little as possible besides changing the PTV. Special effort was made to keep the dose to 98% of the PTV consistent between the three plans. All plans were generated for the Varian Clinac iX linear accelerator with 6 MV photons.

Dose Calculation

To assess the ability of the different margins to account for setup variability, dose calculations were performed on CBCT images for each of the three plans. In order for dose-volume metrics to accurately reflect a subject's position on a given treatment day, bowel and bladder contours were redrawn on each CBCT used in the study. Although the small bowel contour was used for planning purposes, a bowel structure that included both colon and small

bowel was used for dose comparison with pre-treatment CBCTs. This was necessary as colon and small bowel can be indistinguishable on lower quality CBCT images, which often contain more image artifacts.

In order to create the CTV contours on each CBCT, a rigid auto-registration was performed between the CT simulation and CBCT images, based on the position of the patient's sacrum. The CTV contour was then copied onto the CBCT. This process kept the CTV shape and size unchanged while adjusting the pitch, yaw and roll to match the treatment position. The quality of each registration was assessed individually by two separate planners. Degrees of pitch, yaw and roll discrepancy between initial CT simulation and each pre-treatment CBCT were recorded.

The three plans for each subject were then copied onto each daily CBCT and dose was calculated on these image sets utilizing Varian's Anisotropic Analytical Algorithm (AAA) (Figure 3). The Hounsfield Unit (HU) to density calibration curve for CBCTs is highly variable based on patient anatomy, therefore the derived dose-volume metrics are not absolute and are used only to create relative comparisons between the three plans on a given pretreatment CBCT. Comparison of CTV coverage is the primary means of assessing the different planning margins, but OAR metrics are also important when evaluating the clinical impacts of increased margins. For each subject, three dose-volume metrics were recorded for each plan on each pretreatment CBCT: percent volume of CTV receiving 98% of the prescription dose (CTV V98%[%]), absolute volume (cubic centimeters) of bowel receiving 45 Gy (Bowel V45Gy[cc]), and absolute volume (cc) of bladder receiving 40 Gy (Bladder V40Gy[cc]).

Statistical Analysis

Statistical analysis was performed using the GENMOD procedure in IBM SAS v.9.4. A repeated measure Analysis of Variance (ANOVA) test with covariates was performed. The

repeated measure is each subject's individual pretreatment CBCT. The covariates are the three measures of setup discrepancy: pitch, yaw and roll. The test was performed separately for each output dose-volume metric: CTV V98%[%], Bowel V45Gy[cc] and Bladder V40Gy[cc]. Comparisons of generalized estimating equation (GEE) parameters and their 95% confidence intervals (CI) were used to compare the differences between the three plans for a given dose metric, with a $p < .05$ indicating a significant difference. Wald statistics were calculated for each of the covariates, with $p < .05$ indicating that changes in that covariate (pitch, yaw or roll) significantly impacted the variance in the dose metric between the three plans.

Results

The goal of this study is to evaluate the effects of three different axial CTV-PTV margins on target coverage when using VMAT to treat rectal cancer prone on a belly board device. The data of seven previously treated rectal cancer patients was used to perform this analysis.

Setup Variation

Setup variations were recorded for each of the pretreatment CBCTs analyzed in this study. The setup variations were quantified as degrees of difference between the original CT simulations and pretreatment CBCTs in three rotational axes: pitch, yaw and roll. The Eclipse TPS rigid autoregistration software was used to register the images based on sacrum and pelvis position.

The average daily setup variation (degrees) for each patient can be seen in Table 1. The average daily setup variation across all patients was 2.86, 0.95 and 1.36 degrees for pitch, yaw and roll, respectively. The greatest variation was seen in pitch with a minimum value of 0.0 degrees and a maximum of 7.6 degrees. There was less variation in roll with a minimum value of 0.0 and

a maximum of 4.1 degrees. Yaw showed the least variation with a minimum value of 0.0 degrees and maximum of 2.1 degrees (Figure 4).

CTV Coverage

The CTV volumes for each patient ranged from 500.0 cc to 905.0 cc, with a mean volume of 721.6 cc across all subjects. Percent volume of CTV receiving 98% of the prescription dose (CTV V98%[%]) was used to evaluate the extent of coverage across the three plans (0.5, 0.8 and 1.0 cm axial CTV-PTV margins). This metric was measured by calculating and averaging the dose using pretreatment CBCT imaging. The average CTV V98%[%] for each plan can be seen in Table 2. The average difference in CTV V98% between the 0.8 and 0.5 cm plans, across all subjects, was 1.08%. The average difference in CTV V98% between the 1.0 and 0.5 cm plans, across all subjects, was 1.52% (Figure 8).

Statistical analysis was performed using the GENMOD procedure in IBM SAS v.9.4. A repeated measure Analysis of Variance (ANOVA) test with covariates was performed. Wald statistics for the GEE analysis indicated that pitch significantly affected the difference in CTV coverage between the three plans, $p < .0001$, $\chi^2 = 55.5$ (Figure 5). Neither yaw nor roll had a significant effect on CTV coverage between the plans, $p = 0.73$ and $p = 0.93$, respectively (Figures 6 and 7).

Analysis of GEE parameters provided estimates of the difference in CTV coverage between the three margins if they were utilized in the general population. Between the 0.5 cm and 0.8 cm plans, it was estimated that there would be a 0.97% increase in CTV V98%, SE 0.125, 95% CI 0.73-1.22%. This indicated a significant difference in CTV V98% between 0.5 cm and 0.8 cm plans, $Z = 7.42$, $p < .0001$. Between the 0.5 cm and 1.0 cm plans, it was estimated that there would

be a 1.41% increase in CTV V98%, SE 0.187, 95% CI 1.04-1.77%. This indicated a significant difference in CTV V98% between 0.5 cm and 1.0 cm plans, $Z = 6.99$, $p < .0001$.

Bowel Dose

The bowel volumes for each patient ranged from 685.58 cc to 2141.02 cc at time of CT simulation, with a mean volume of 1288.72 cc across all subjects. The volume of bowel (cc) receiving at least 45 Gy (Bowel V45Gy[cc]), was used to evaluate the bowel dose across the three plans (0.5, 0.8 and 1.0 cm axial CTV-PTV margins). This metric was measured by calculating the dose using pretreatment CBCT imaging. The average Bowel V45Gy[cc] for each plan can be seen in Table 3. The average difference in Bowel V45Gy between the 0.8 and 0.5 cm plans, across all subjects, was 3.15 cc. The average difference in Bowel V45Gy between the 1.0 and 0.5 cm plans, across all subjects, was 5.17 cc.

In the population, between the 0.5 cm and 0.8 cm plans, it was estimated that there would be a 4.82 cc increase in Bowel V45Gy, SE 0.86, 95% CI 3.13-6.52 cc. This indicated a significant difference in Bowel V45Gy between 0.5 cm and 0.8 cm plans, $Z = 5.59$, $p < .0001$. Between the 0.5 cm and 1.0 cm plans, it was estimated that there would be an 8.91 cc increase in Bowel V45Gy, SE 1.86, 95% CI 5.25-12.56 cc. This indicated a significant difference in Bowel V45Gy between 0.5 cm and 1.0 cm plans, $Z = 4.78$, $p < .0001$.

Bladder Dose

The bladder volumes for each patient ranged from 54.26 cc to 285.04 cc at time of simulation, with a mean volume of 145.35 cc across all subjects. The volume of bladder (cc) receiving at least 40 Gy (Bladder V40Gy[cc]), was used to evaluate the bladder dose across the three plans (0.5, 0.8 and 1.0 cm axial CTV-PTV margins). This metric was measured by calculating the dose using pretreatment CBCT imaging. The average Bladder V40Gy[cc] for each

plan can be seen in Table 4. The average difference in Bladder V40Gy between the 0.8 and 0.5 cm plans, across all subjects, was 4.96 cc. The average difference in Bladder V40Gy between the 1.0 and 0.5 cm plans, across all subjects, was 10.12 cc.

In the population, between the 0.5 cm and 0.8 cm plans, it was estimated that there would be a 4.79 cc increase in Bladder V40Gy, SE 0.63, 95% CI 3.55-6.03 cc. This indicated a significant difference in Bladder V40Gy between 0.5 cm and 0.8 cm plans, $Z = 7.59$, $p < .0001$. Between the 0.5 cm and 1.0 cm plans, it was estimated that there would be a 9.90 cc increase in Bladder V40Gy, SE 1.21, 95% CI 7.54-12.27 cc. This indicated a significant difference in Bladder V40Gy between 0.5 cm and 1.0 cm plans, $Z = 8.22$, $p < .0001$.

Discussion

The purpose of this study was to evaluate the ability of different CTV-PTV margins to account for the increased setup variability when using the prone bellyboard position to treat rectal cancer. The results of this study indicated a statistically significant difference in CTV V98% coverage between the three plans evaluated, with a correspondingly significant increase in OAR doses. Closer consideration is necessary to determine whether or not the magnitude of these differences would have any clinical impact.

CTV Coverage

Utilization of the 1.0 cm margin lead to a 1.4% increase in CTV 98%, indicating a greater homogeneity of dose throughout the CTV. Greater homogeneity of dose throughout the target volume has been shown to increase tumor control probability[28]. However, some propose using less conservative coverage constraints dictating CTV coverage of 99% of the target volume by

95% of the prescription dose[29]. All three of the plans and their accompanying margins were able to account for setup variation within this tolerance.

Bowel & Bladder Doses

RTOG 0822 recommends keeping Bowel V45Gy dose under 65 cc[21]. The difference between the 0.5 and 1.0 cm plans was an increase of Bowel V45Gy of 5.25-12.56 cc. Even with this increase in dose, well designed VMAT plans with 1.0 cm axial margins can keep the bowel dose below RTOG 0822 tolerances.

Bladder doses increased correspondingly between the 0.5 and 1.0 cm plans, with an increase of Bladder V40Gy of 3.55-6.03 cc. RTOG recommends keeping Bladder V40Gy under 40%[21]. Bladder constraints could limit the use of 1.0 cm axial margins if the patient has particularly poor bladder filling. In these cases, the 1.0 cm axial margin can be cropped out of the bladder by 0.2 to 0.5 cm to maintain the benefits in CTV coverage at the superior and inferior ends of the target volume while reducing bladder dose.

Limitations

The length of CBCT scans limits the accuracy of dose calculations at the superior and inferior ends. Even though the CTV was contained within the scan length in all of these cases, the lack of lateral scatter near the edges of the scan volume resulted in lower calculated dose to these areas. While this effect was the same for each scan across the three plans of different margins, the area where the effect of pitch and yaw would be most pronounced is near the ends of the CTV. The lack of dose calculation accuracy in these areas might have led to an underestimation of the effects of the larger margins on CTV coverage.

The nature of inverse planning makes it impossible to create VMAT plans in the Eclipse TPS that are exactly alike with the exception of CTV-PTV margin. The initial symmetrical 0.5

cm margin plan was created first, and every effort was made to keep the subsequent plans as alike as possible. However, within the plan optimizer, the MLC sequence was out of the planner's control, creating variation in the three plans beyond what would be seen if the margins were changed in a simple 3DCRT plan.

Conclusion

External beam radiation for the treatment of rectal cancer has the potential to induce small bowel toxicity[9]. Treating rectal cancer patients prone on a bellyboard device reduces small bowel doses[10]. However, utilization of the bellyboard device increases daily setup variability[11]. VMAT techniques further decrease small bowel doses, but allow less room for error in patient setup[23]. PTVs utilized in VMAT plans need to adequately account for any increased setup variations when using the bellyboard device.

This study evaluated three different plans with varying CTV-PTV margins. The first with symmetrical 0.5 margins, the second with 0.5 craniocaudal margins and 0.8 cm axial margins and the third with 0.5 cm craniocaudal margins and 1.0 cm axial margins. Compared to the 0.5 cm axial margin, the 1.0 cm axial margin resulted in a statistically significant increase in the CTV V98% by 1.04-1.77%. Bowel V45Gy and Bladder V40Gy were also increased by 5.25-12.56 cc and 7.54-12.27 cc, respectively. These results indicate that if the goal is greater prescription dose coverage of the CTV, 1.0 cm margins can be used with minimal increase in OAR volumes receiving near prescription doses.

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Table 1. Average Daily Setup Variations Across Pretreatment CBCTs by Subject With Standard Deviation

Subject	Pitch (deg)	Yaw (deg)	Roll (deg)
	Mean (SD)	Mean (SD)	Mean (SD)
1	3.65 (1.96)	0.97 (0.43)	1.08 (0.82)
2	4.45 (1.34)	0.72 (0.67)	0.42 (0.45)
3	5.28 (2.13)	0.67 (0.43)	1.07 (0.71)
4[a]	0.42 (0.37)	0.96 (0.45)	0.86 (0.73)
5	1.28 (0.83)	1.34 (0.59)	0.52 (0.32)
6	3.10 (0.90)	1.17 (0.48)	3.52 (0.52)
7	1.13 (0.68)	0.92 (0.83)	1.83 (0.58)
Total	2.86 (2.05)	0.95 (0.57)	1.36 (1.18)

[a]Only 5 pretreatment CBCTs were available for this subject.

Table 2. Average CTV V98%[%] Across CBCTs for Each Plan by Subject With Standard Deviation

Subject	0.5 cm Plan	0.8 cm Plan	1.0 cm Plan
1	95.55 (1.96)	96.17 (1.85)	96.72 (1.74)
2	97.42 (1.23)	98.08 (0.97)	98.30 (0.85)
3	94.32 (1.72)	95.23 (1.40)	96.00 (1.19)
4	98.19 (0.95)	99.45 (0.37)	99.59 (0.34)
5	98.18 (0.95)	98.77 (0.56)	98.86 (0.44)
6	96.72 (0.81)	98.56 (0.59)	98.84 (0.33)
7	97.11 (2.04)	98.35 (1.31)	99.46 (0.50)
Total	96.78 (1.42)	97.80 (1.52)	98.25 (1.37)

Table 3. Average Bowel V45Gy[cc] Across CBCTs for Each Plan by Subject With Standard Deviation

Subject	0.5 cm Plan	0.8 cm Plan	1.0 cm Plan
1	23.47 (4.35)	26.65 (3.19)	29.66 (3.30)
2	320.98 (28.64)	339.89 (31.22)	358.90 (32.71)
3	8.76 (5.03)	10.63 (5.88)	13.64 (6.63)
4	92.44 (19.30)	96.33 (20.01)	95.34 (19.61)
5	53.83 (8.04)	56.84 (8.03)	58.31 (8.20)
6	50.67 (10.87)	54.84 (12.35)	53.17 (11.55)
7	42.12 (22.18)	44.92 (23.92)	49.52 (26.93)
Total	84.61 (107.49)	90.01 (113.41)	94.08 (119.51)

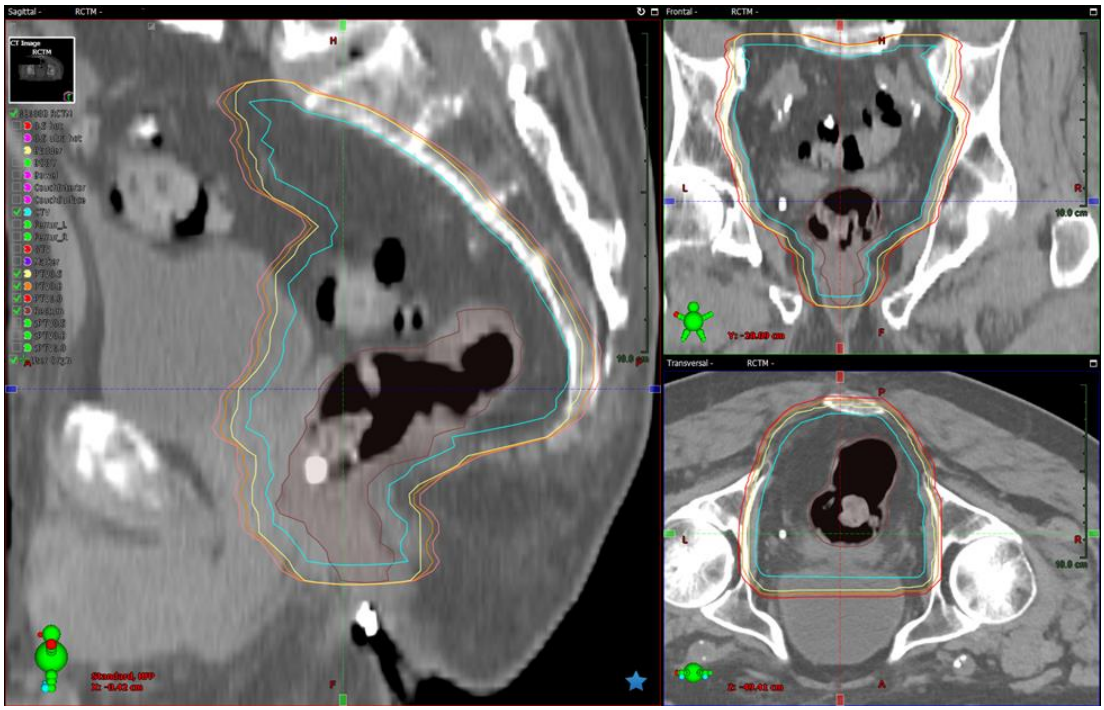
Table 4. Average Bladder V40Gy[cc] Across CBCTs for Each Plan by Subject With Standard Deviation

Subject	0.5 cm Plan	0.8 cm Plan	1.0 cm Plan
1	13.33 (6.52)	17.28 (8.35)	20.97 (9.51)
2	6.36 (2.30)	10.45 (1.97)	14.14 (2.44)
3	9.42 (8.12)	12.02 (10.67)	15.78 (13.91)
4	15.58 (6.36)	20.53 (7.04)	26.10 (7.48)
5	10.74 (8.16)	16.48 (9.92)	20.18 (11.00)
6	29.10 (12.56)	34.31 (14.02)	42.17 (15.23)
7	70.69 (40.88)	82.97 (45.83)	94.38 (50.11)
Total	22.17 (22.61)	27.72 (25.59)	33.39 (28.46)

Figure 1. CIVCO Carbon Fiber Bellyboard

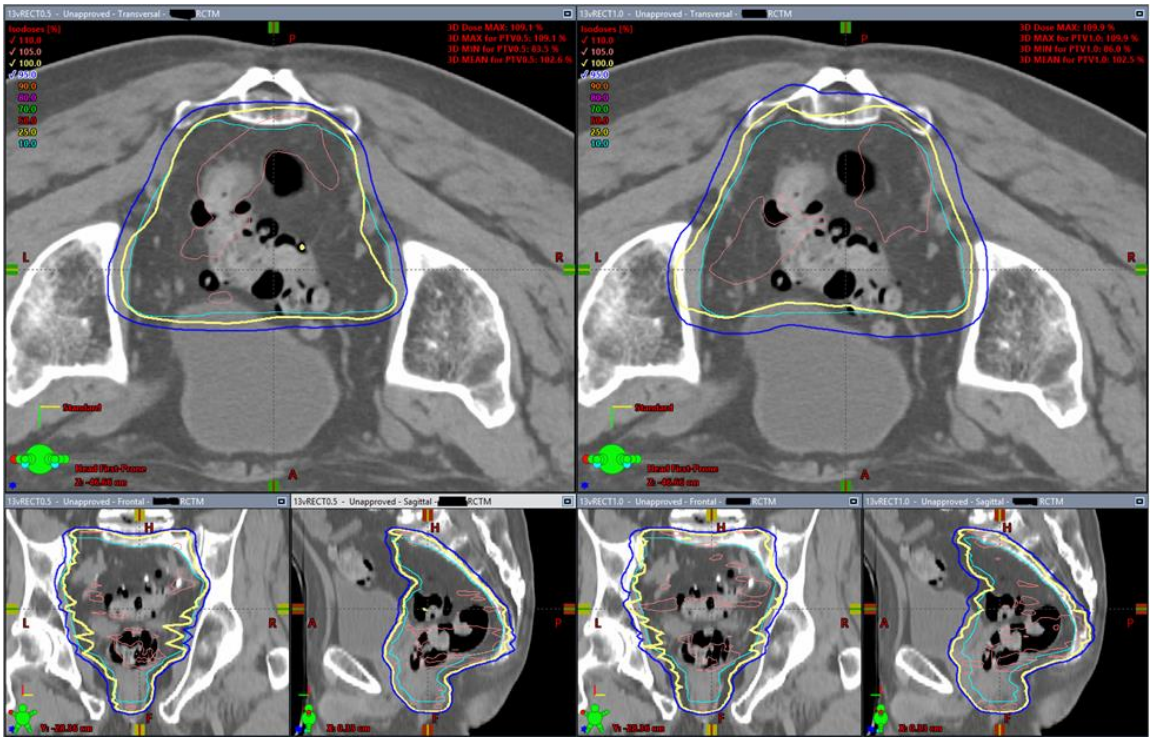
CIVCO Radiotherapy. http://civcort.com/ro/hip-pelvic-positioning/bellyboards

Figure 2. Depiction of the Three Different PTV margins in Eclipse TPS



Cyan = CTV, Yellow = PTV 0.5cm, Orange = PTV 0.8cm, Red = PTV 1.0cm

Figure 3. Comparison of Two Plans for a Subject Calculated on Simulation Data Set and CBCT Data Set



Plan 0.5cm (Left) & Plan 1.0cm (Right), Simulation Data Set

Figure 4. Boxplot of Degrees of Variation by Rotational Direction

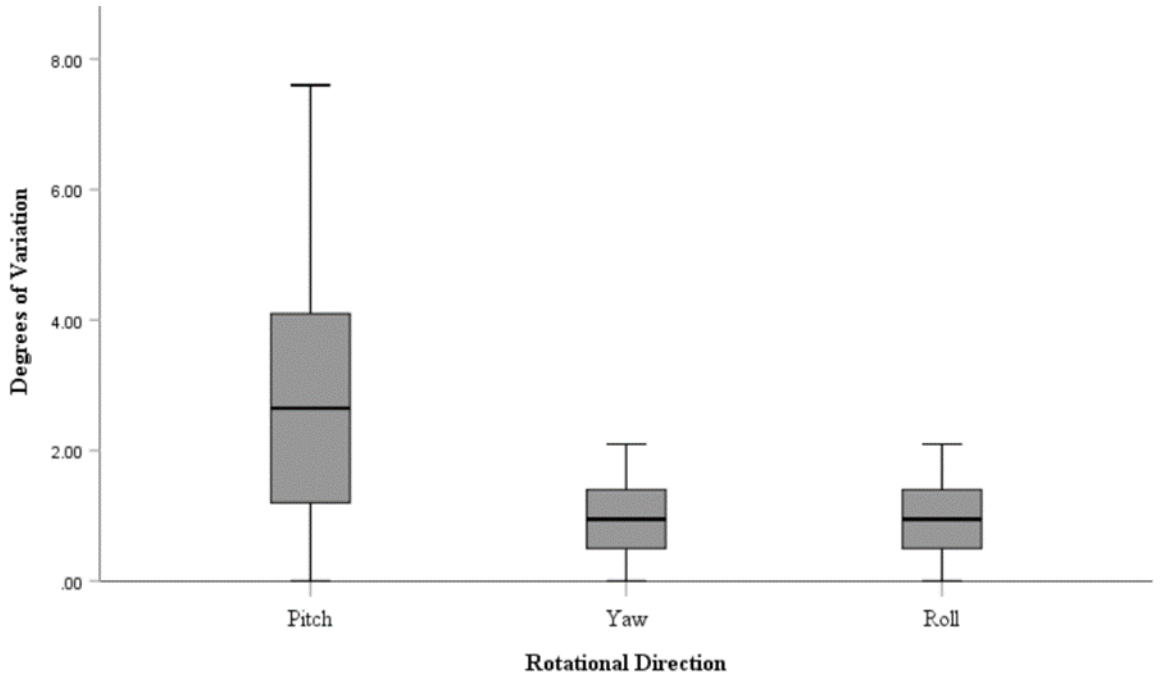


Figure 5. Predictive Value of Pitch on CTV V98%[%] ($p < .0001$).

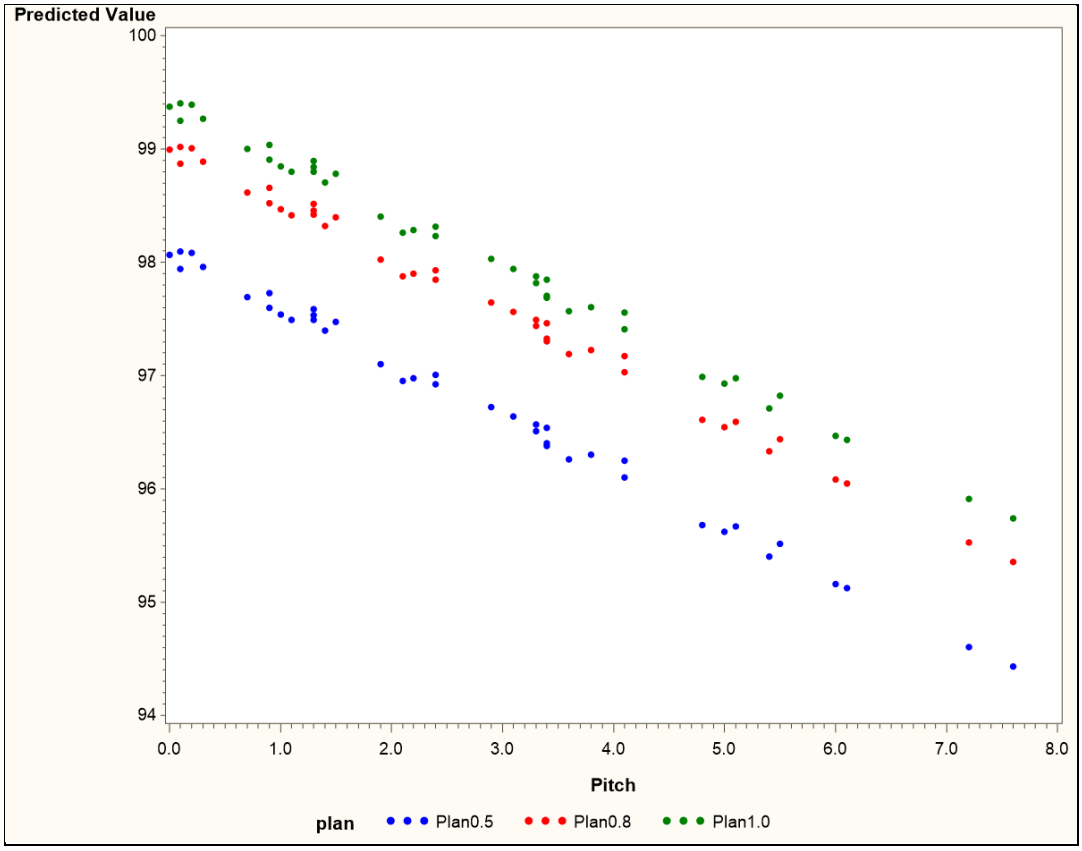


Figure 6. Predictive Value of Yaw on CTV V98%[%] (p = 0.73).

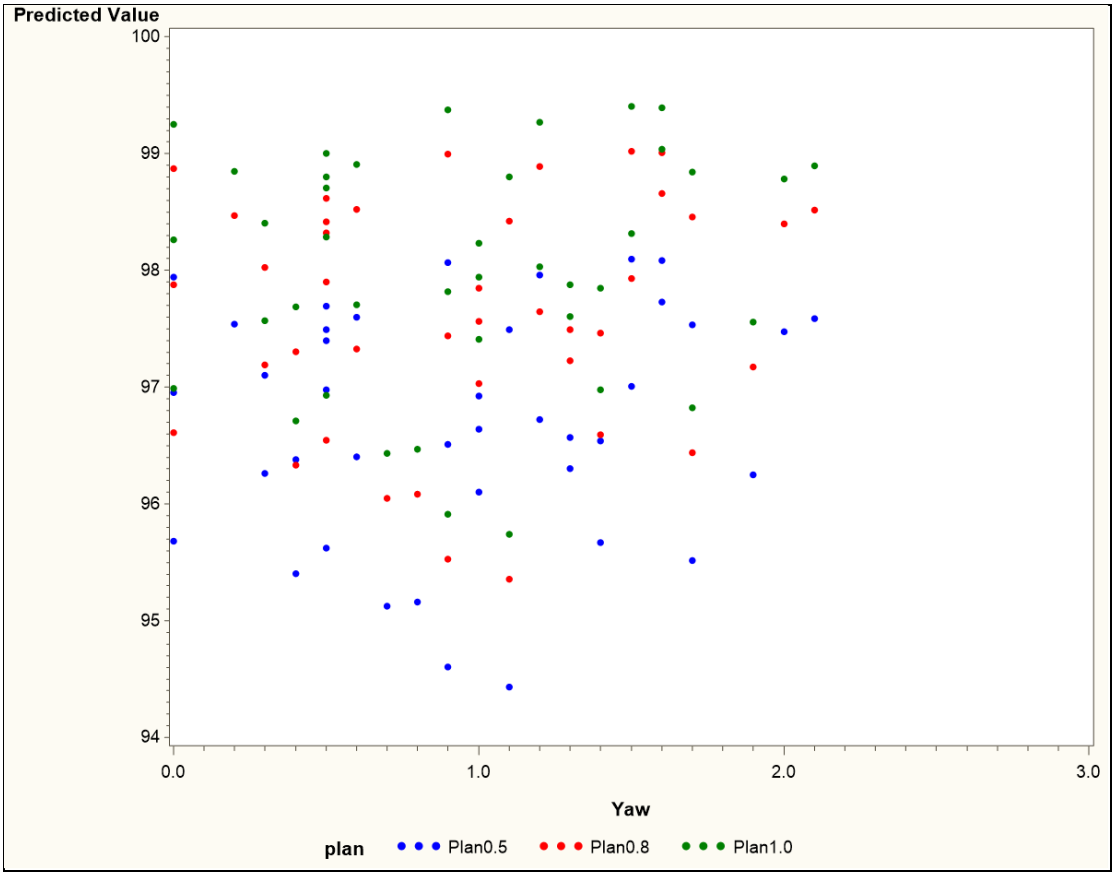


Figure 7. Predictive Value of Roll on CTV V98%[%] (p = 0.93).

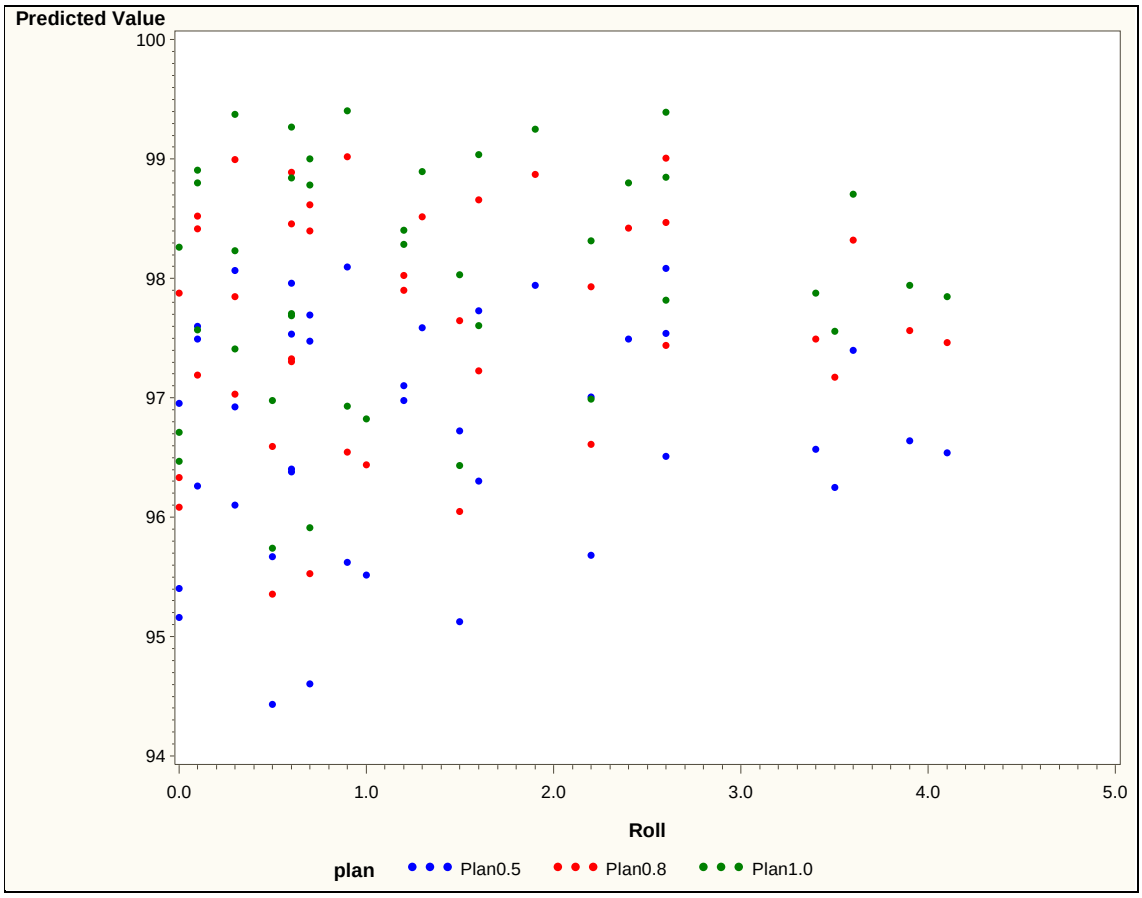


Figure 8. Boxplot of CTV V98%[%] by Plan