Impact of pitch angle setup error and setup error correction on dose distribution in volumetric modulated arc therapy for prostate cancer

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Impact of Pitch Angle Setup Error and Setup Error Correction on Dose Distribution in Volumetric Modulated Arc Therapy for Prostate Cancer

Running Title: Impact of Pitch Angle Error and Setup Error Correction in VMAT

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Abstract

In volumetric modulated arc therapy (VMAT) for prostate cancer, a positional and rotational error correction is performed according to the position and angle of the prostate. The correction often involves body leaning, and there is concern regarding variation in the dose distribution. Our purpose in this study was to evaluate the impact of body pitch rotation on the dose distribution regarding VMAT. Treatment plans were obtained retrospectively from eight patients with prostate cancer. The body in the computed tomography images for the original VMAT plan was shifted to create VMAT plans with virtual pitch angle errors of ±1.5 and ±3 degrees. Dose distributions for the tilted plans were recalculated with use of the same beam arrangement as that used for the original VMAT plan. The mean value of the maximum dose differences in the dose distributions between the original VMAT plan and the tilted plans was 2.98 ± 0.96%. The value of the homogeneity index for the planning target volume (PTV) had an increasing trend according to the pitch angle error, and the values of the D_{95} for the PTV and D_{2ml}, V_{50}, V_{60} and V_{70} for the rectum had decreasing trends ($p<0.05$). However, there was no correlation between differences in these indexes and the maximum dose difference. The pitch angle error caused by body leaning had little effect on the dose distribution, in contrast, the pitch angle correction reduced the effects of organ displacement and improved these indexes. Thus, the pitch angle setup error in VMAT for prostate cancer should be corrected.

Keywords

volumetric modulated arc therapy, prostate cancer, setup error, dose distribution, pitch angle

1. INTRODUCTION

Many patients with prostate cancer are treated with precision irradiation techniques such as intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). IMRT and VMAT require high-precision patient setup to ensure accurate radiation dose delivery. However, positional uncertainties regarding the prostate exist as a result of variations in the inter- and intra-fractional position. Schallenkamp et al. [1] evaluated the relationship between the position of a gold marker implanted in the prostate and that of the pelvic bones. They found that the position of the prostate was not related to the position of the pelvic bones. Ghilezan et al. [2] found that the degree of prostate motion depended on the volume of feces in the rectum. In other words, the prostate moves independently in the body, and its motion depends on the rectal volume.

Prostate motion consists of translations and rotations. The translational positional error of the prostate during a treatment course or during a single treatment session has been assessed previously in many studies [3-6]. Rotational error has also been evaluated with use of an in-room computed tomography (CT) system [7]. The standard deviations of inter-fractional rotations around the lateral and superior-inferior axes were found to be approximately 8 degrees when measured with implanted markers. However, in measurements involving the contoured prostate in the CT images, the standard deviation of inter-fractional rotations around the lateral axis was reported to be approximately 10 degrees [7]. Hoogeman et al. [8] evaluated prostate motion with a view to reducing rotational motion effects, and that found that the rotation around the lateral axis was the largest of the rotations around the three coordinate axes. Thus, rotation around the lateral axis (referred to as pitch rotation) of a prostate should be of concern in high-precision radiotherapy.

The effects of setup error, including rotational errors, on the dose distribution during commonly used radiation therapies have been evaluated for several body sites [9]. The

dosimetric effect of rotational setup errors concerning IMRT for head and neck cancer has also been evaluated [10]. Cranmer-Sargison reported the dosimetric impact of rotational error in three-dimensional conformal radiation therapy for prostate cancer [11]. Rotational errors around the lateral and anterior-posterior axes had a greater effect on the dose distribution than did the other types of rotation error. The impact of rotational error regarding the treatment of prostate cancer with VMAT has not yet been evaluated, and our preliminary study showed that pitch angle error affected the dose distribution more than did the other angle errors [12]. For avoiding this impact of rotational setup errors, adding additional margins for rotational setup errors to clinical target volume (CTV) is a solution, however, the calculation of the margin for rotational setup errors is very complicated, so that many institutions would not add such a margin to CTVs[13].

McNair et al. [14] compared setup error correction methods by using the bony anatomy and gold markers implanted in the prostate. Corrections made by means of the gold markers resulted in a more accurate setup than did those made based on the bony anatomy. Presently, six-degrees-of-freedom robotic couches are used for setup error correction. Such a couch can lean by approximately ±3 degrees. When the rotational error regarding the prostate is corrected with a robotic couch, the surface of the body will lean because the prostate moves independently of the patient's body in almost all cases. In such cases, there is concern that this lean might change the dose distribution in the body.

Deformation of the rectum as a result of volume change should affect the dose distribution and the dose to the organs more than does the setup error alone. Ghilezan et al. [2] found that prostate motion would be produced by the deformation of the rectum; this means that the impact of rectum deformation on the dose distribution could include the impact of prostate motion. It is important to evaluate the impact of each of the factors. However, certain categorization or quantitation of the deformation is not an easy task. We focused on the

impact of prostate motion, especially pitch angle rotation.

In summary, pitch angle errors that involve rotation around the lateral axis constitute the major rotational error associated with cancer treatment of prostate, and its effects on the dose distribution of VMAT treatment plans have not been evaluated. Although rotational error can be corrected with a six-degrees-of-freedom robotic couch, there is concern about varying the dose distribution as a result of body surface leaning.

In the present study, we evaluated the impact of the pitch angle error with regard to the dose distribution in VMAT, including the effects of body leaning associated with pitch angle error correction.

2. MATERIALS AND METHODS

VMAT plans from eight cases involving local prostate cancer were evaluated retrospectively in this study. The median age of the patients was 67 (range, 60–83) years, and the clinical stages ranged from stage II to stage IV. Two of the eight patients had received treatment involving a combination of permanent implantation of 125-I seeds and VMAT for the prostate. Three patients were treated with a combination of whole pelvis irradiation and VMAT, and the remaining patients were treated with VMAT with irradiation restricted to the prostate only. The patient position was prone in six cases and supine in the other two. The number of fractions administered ranged from 12 to 38, and the total doses delivered ranged from 24 to 76 Gy. For all treatment plans, the prostate was contoured as the CTV and the CTV to planning target volume (PTV) margin was 0.5 cm on the posterior side of the prostate and 0.8 cm on the other sides. The isocenter was placed at the center of the PTV. This study was approved by the institutional review board for the collection and use of patient treatment planning data.

Several studies have simulated the rotational setup errors by arrangement of the beam

alignment [9-11]. This is possible for a treatment plan with fixed beams such as a fixed beam IMRT plan. However, a VMAT plan has a rotating beam, so that the patient body in the CT images has to be rotated. Additionally, if the body has to be rotated three-dimensionally, an interpolation process is necessary for the production of the CT slice images. The interpolation process might make the volume of the contours such as the PTV and rectum vary. Thus, in the present study we shifted the body in the CT images according to the pitch angle. With this method, the contours are not deformed and the volume of the contours can be maintained for comparison. Then, the radiation treatment planning system (TPS; Monaco Ver. 4: Elekta, Crawley, UK) that we used can calculate the dose distribution without volume change of the contours, so that the dose and volume indexes for the tilted plan can be compared with those for the original one because the indexes are based on the same volume.

For direct evaluation of the effect of body leaning, the prostate in the CT images should be rotated independently of the other anatomy. However, prostate rotation will result in the need for rectum or bladder deformation, and such deformation of the anatomy is not known. Anatomic structure deformation makes comparison of the dose to the target structure complicated because of the volume change. Therefore, we decided to discuss the effect of body leaning on the results obtained with this method.

The CT images for all original VMAT plans were acquired with a Toshiba Aquirion L/B (Toshiba Medical Systems, Ohtawara, Japan) operating at 120 kV and 100 mA, with a 3-sec rotation and a slice thickness of 2 mm. The CT image had a matrix size of 512 × 512 and a field of view 40 cm in diameter. The VMAT plans were used for clinical treatment, and all patients completed their treatments.

A CT image set with a pitch angle error was created with the original CT image set used in patient treatment. The virtual pitch angle errors were ±1.5 and ±3 degrees based on the original VMAT plan. A maximum angle of ±3 degrees was selected because robotic couches

in hospitals can correct the angle setup error in that range. The direction of rotation is shown in Fig. 1.

For creating a CT image set with a pitch angle setup error, the body and all structures such as the PTV and the rectum in each CT image slice were moved up or down in the slice by distances d_1 and d_2 (Fig. 2), according to the pitch angle. The center of rotation was the isocenter. For moving the body up, several top rows equivalent to d_1 of the CT image matrix were removed. Several top rows of the matrix were added for moving the body down. The structures were moved manually corresponding to the distance equivalent to d_1 and d_2 to fit the shifted body in each CT image. With use of this method, it was possible to maintain the volume.

There was a difference in the superior-inferior (SI) direction between a position that was actually rotated and one shifted in a plane. Our tilted plans did not take into account this difference in the SI direction (Fig. 2). However, the distance between these two positions was not significantly large. The distance can be calculated as follows:

$$e = d(1-\cos\theta), \qquad (1)$$

where e is the distance in the SI direction between the rotated and shifted positions in an image and d is the distance from the rotation center to a point that was rotated or shifted. θ is the pitch angle setup error. When d = 30 mm, e is 0.04 mm. The length of 30 mm was the average half length of the prostate in the SI direction in the current study, the length being about 60 mm. Even if d = 60 mm, e = 0.08 mm. That distance was smaller than the pixel size of the CT images.

A tilted plan was created by use of one of the CT image sets with a virtual pitch angle error and the same beam arrangements as those of the original plan, and the dose distribution

was recalculated for the tilted plan. Calculation of the dose distribution for all plans was performed with the use of the TPS. The dose distribution was computed by means of the Monte Carlo method, with a dose variance of 3% and a calculation grid size of 3×3 mm^2, because these parameters were used clinically and the original plan had been calculated with the same parameters. The plan and its dose distribution, which was approved by a radiation oncologist, were treated as the reference so that the tilted plans could be calculated with use of the same parameter values.

The maximum differences in the dose between the dose distribution of the original plan and that of a tilted one were obtained. Dose distribution data were exported from the TPS to files in the digital information and communication in medicine extension for radiation therapy (DICOM-RT) format. The dose difference was calculated by subtracting of the dose data obtained from the DICOM-RT files of the original plan from the dose data of the tilted plan.

To compare the doses to normal tissues (rectum and bladder) and targets (CTV and PTV), we evaluated dose indexes for the targets and normal tissues and volume indexes for normal tissues on each plan. The dose indexes for the CTV and PTV were the homogeneity index (HI), median dose (D_{med}), the dose at 95% volume (D_{95}) and the dose at 2% volume (D_2). Use of D_2 as the maximum dose was recommended in the International Commission on Radiation Units and Measurements Report 83 [15]. The dose to the CTV and PTV was normalized by the total dose for each patient and was represented as a percentage based on the total dose. The range of total doses for the cases was 24–76 Gy. Several definitions of the HI are available. The HI that we used is defined as

$$HI = \frac{D_2 - D_{98}}{D_{50}}, \qquad (2)$$

where D_{98} is the dose to a structure where 98% of the volume of the structure receives more than this dose, and D_{50} are the doses delivered to 50% of the volume of a structure.

The dose indexes and volume indexes for the rectum and bladder were D_{med} and $D_{2ml,}$ and the volumes that received more than 40 Gy (V_{40}), 50 Gy (V_{50}), 60 Gy (V_{60}), and 70 Gy (V_{70}) were obtained. The D_{2ml} is the dose to a volume of 2 ml of the rectum or the bladder. To calculate the dose and volume indexes for the bladder and rectum, we rescaled the prescribed dose for the plans as 76 Gy, and the dose indexes for the bladder and rectum were expressed in Gy. High-dose delivery to the rectum can cause bleeding, so that volumes with high-dose exposure such as the V_{60} and V_{70} are important indexes for prognosis regarding side effects. All dose and volume indexes were tested statistically with use of the Kruskal–Wallis test [16], which is a non-parametric method for testing differences among more than two groups; the significance of the trend for each of the dose and volume indexes that depended on the pitch angle error was confirmed by use of the Jonckheere–Terpstra test [17].

Maximum dose differences between the dose distributions of the tilted plans and that of the original one were obtained, and differences of the dose or volume index values for the tilted plans from the corresponding value of the original plan was obtained. The correlation between the difference of the index values and the maximum dose differences was investigated. The indexes which demonstrated the statistical significance by the Jonckheere–Terpstra test were used for investigation of the correlation.

3. RESULTS

Results of the dose and volume index for CTV, PTV, bladder, and rectum are shown in Fig. 3, 4, 5 and 6, respectively. There was no significant difference in the dose and volume indexes regarding the tilted plans at each pitch angle as determined by the Kruskal-Willis test ($p > 0.05$). However, by the Jonckheere-Terpstra test, values for the D_{95} ($p=0.036$) for the PTV

(Fig. 4) and D_{2ml} (p=0.015), V_{50} (p=0.037), V_{60} (p=0.030), and V_{70} (p=0.011) for the rectum (Fig. 6) had a significant decreasing trend according to the pitch angle error, and values for the HI (p=0.005) for the PTV (Fig. 4) had a significant increasing trend.

The maximum dose difference was obtained by subtraction of each dose distribution for the original plan from that for the tilted one. In the front or back skin area, the subtracted dose was relatively higher/lower than the subtracted dose in the middle portion of the body; this was because the dose difference at these skin areas represented the difference between the dose to tissue and the dose to air. The dose differences in these skin areas were not included in the calculation of the maximum dose difference. The subtracted dose that represented the difference in the dose distribution of the −3 degrees tilted plan from that of the original one overlying the original CT image is shown in Fig. 7 as an example. This case had the largest value (5.62%) of the maximum dose difference of all the cases; the dose was represented as a percentage based on the total dose for this patient. The mean of the maximum dose difference was 2.98% for all tilted plans, and the maximum dose difference ranged from 0.03 to 5.62%. The mean value for the 1.5-degree tilted plans was 2.73%, and that for the 3-degree tilted plans was 3.22%. The maximum dose difference values for the 1.5-degree tilted plans for all cases did not exceed 4%. The maximum dose difference values for the 3-degree tilted plan for five cases (62.5%) did not exceed 4%, and only one case had >5%. The location of the maximum dose difference was around the PTV.

Absolute differences in the HI and D_{95} for the PTV (ΔHI and ΔD_{95}, respectively) and the D_{2ml}, V_{50}, V_{60}, and V_{70} for the rectum (ΔD_{2ml}, ΔV_{50}, ΔV_{60}, and ΔV_{70}, respectively) for the tilted plan were calculated from these values for the original plan. No correlation was found between the ΔHI, ΔD_{95}, ΔD_{2ml}, ΔV_{50}, ΔV_{60}, and ΔV_{70} and the maximum dose difference (Fig. 8). The best correlation coefficient was -0.227 for the PTV ΔHI (Fig. 8b).

4. DISCUSSION

There were no appreciable differences in dose distribution between the tilted and original treatment plans. The mean value of the maximum dose difference was only 2.98%, and even for the 3-degree tilted plans it was only 3.22%. This value is similar to the dose variance of 3% obtained with use of the Monte Carlo dose calculation.

Regarding all of the dose and volume indexes for all structures, there were no significant differences among the tilted and original plans. However, there was a trend for increasing values of the HI for the PTV, and a trend for decreasing values for the PTV D_{95} and the rectum D_{2ml}. Differences regarding the PTV D_{95} and rectum D_{2ml} between the ±3-degree tilted plans were 0.70% and 0.71%, respectively. The HI was calculated from the D_2, D_{98}, and D_{50}. The D_{50} was almost equal to the D_{med}. Values for the D_{med} and D_2 for the PTV did not change with the pitch angle. Thus, the D_{98}, which was close to the D_{95}, affected the HI for the PTV.

There was a trend for decreasing values of the V_{50}, V_{60}, and V_{70} for the rectum. The difference between the mean values for the ±3-degree tilted plans for the V_{50}, V_{60}, and V_{70} was approximately 1.8 ml. The mean volume of the rectum was 47.2 ml, and thus this 1.8 ml difference represents approximately 4% of the rectal volume. The RTOG-0415 study [18] applied a dose limit for the rectum that, for the V_{70}, should not exceed 25% of the volume. Fiorino et al. [19] found that, if V_{70} was <30%, the frequency of late rectal bleeding decreased significantly. The range of V_{70} values for the rectum in the original plans in the present study was 2.9–7.7 ml (8.2–18.2%), and these values were lower than the RTOG-0415 dose limit even if the volume of 4% was added to the V_{70}.

Absolute differences in the HI and D_{95} for the PTV and the D_{2ml}, V_{50}, V_{60}, and V_{70} for the rectum between the tilted and original plans had no correlation with the maximum dose difference (Fig. 8). The best correlation coefficient was -0.227 for the PTV ΔHI. Thus, a

change in the dose distribution regarding the pitch angle error would not be associated with a trend for changing values of these indexes.

The reason why the values for the dose and volume indexes for the PTV and the rectum tended to change according to the pitch angle error is that the PTV and rectum moved into low- or high-dose areas in the irradiation field, where the overall dose distribution remained almost unchanged at different pitch angles. The trend of these indexes might depend on the PTV margin. If a large PTV margin is applied, the radiation dose to the PTV will remain unchanged by the pitch rotation, but there will be a greater variation in the radiation dose to the rectum. The maximum dose difference might depend upon the PTV margin because the cases involving a large PTV (>100 ml) had a higher maximum dose difference than did the cases involving a small PTV (<100 ml); the mean values were 3.49% and 2.77%, respectively.

The width of the PTV margin used could affect the results. If a PTV margin includes the effect of the rotational setup error the variation of the dose and volume indexes would be reduced. However, the calculation of the margin for rotational setup errors is very complicated, and the width of the margin would be varied according to the distance from an isocenter. TPSs could not automatically add such a non-uniform margin to a target, so that a planer should do time-consuming task to add the non-uniform margin. Many institutions ignore the rotational variation for the calculation of the PTV margin [13], so that evaluation of the impact of the rotational setup error is still important.

In image-guided radiation therapy, cone beam computed tomography can reveal the prostate, or two-field radiography can detect the position of the prostate and its angle by detecting implanted fiducial markers such as gold coils. In image-guided radiation therapy, it is also possible to use cone beam computed tomography images of the prostate or the fiducial markers to calculate the setup error, instead of the bony anatomy. The setup error calculated

from prostate images often differs from that calculated by means of the bony anatomy. Body leaning of ±3 degrees only makes about a 3% difference at most in the dose distribution in the patient's body. In addition, the HI and D_{95} for the PTV and the D_{2ml}, V_{50}, V_{60}, and V_{70} for the rectum showed that a portion of the prostate or rectum may move into a low- or high-dose area if the setup error is corrected according to the angle calculated from the bony anatomy. Thus, a setup error correction should be carried out in accordance with the angle of organs such as the prostate and rectum in VMAT for prostate cancer.

In the present study, shifting of the body was performed in the CT images instead of true rotation of the body. There is a difference between rotated and shifted positions along the SI direction; this is particularly true regarding the anterior/posterior portion of the body in the isocenter slice. The anterior/posterior portion of the body can have the largest SI positional differences. The difference depends on the rotational angle and the distance from the isocenter, which is the origin of the rotation. The rectum and prostate are shown in the isocenter slice, but the rectum is farther from the isocenter. The mean distance from the isocenter to the anterior rectum wall along the AP direction, to which a higher dose was delivered, was 15.7 mm (all cases). When the body rotation was 3 degrees, the anterior rectum wall (15.7 mm from the isocenter) should be shifted by 0.8 mm along the SI direction. The rectum is long in the SI direction, so that the dose that should be delivered to the rectum in the isocenter plane would be delivered to that in the next slice. Additionally, the difference of 0.8 mm was about a quarter of the calculation grid size (3 mm). Therefore, the dose and volume indexes for the rectum were not appreciably affected by the positional difference in the SI direction around the isocenter slice. The dose and volume indexes for the rectum would be affected mainly by the positional variations along the AP direction in slices near the field boundaries.

Regarding the positional difference between the truly rotated and shifted distal portions of the body, the positional difference could be larger than that for the rectum. The

distal portion of the body should be replaced by a portion of the body in other slices, or interpolated with a portion in other slices if the body was truly rotated. However, such a portion is mainly soft tissue, and the portion in other slices is usually the same tissue, so that the difference at the distal portions did not affect the dose distribution. Only the sacrum bone would have an effect on the dose distribution because it is located near the back and its distal end would be located in the irradiation field. The mean distance between the sacrum bone and the isocenter was about 70 mm along the AP direction. The distance of 70 mm caused a 3.7 mm difference in the SI direction when the rotation angle was 3 degrees. This difference is larger than the calculation grid size. Thus, our results could not include the effect of this displacement of a sacrum bone. For portions located far from the isocenter along the SI direction, these portions mainly move up/down when the body is rotated. Shifting the body in CT images does not cause a large error.

The rectum and prostate can be deformed by the volume of gas and feces in the rectum. The bladder can also be deformed, depending on the amount of urine present. With our method, we cannot evaluate the effects of these organ deformations because it uses only one CT image set for radiotherapy planning and we investigated the impact of body rotation. The dose to the rectum might be changed by the deformation even if the prostate position and rotation is corrected by use of a 6 degrees-of-freedom robotic couch. For instance, if the volume of feces in the rectum increases from at the radiation therapy planning, the volume of the rectum wall receiving a high dose will be reduced because the rectum wall is expanded. This is a favorable example but to obtain such impact and also avoid unfavorable impact, doses to the prostate and surrounding tissue should be delivered as originally planned. According to our findings, moving a portion of an organ into a higher/lower-dose area as a result of organ motion affected dose to the organ, so that the setup error correction corresponding to the motion of the prostate should be applied. The dosimetric impact of organ

deformation depends upon cases. Assessment of the general dosimetric impact of organ deformation is difficult because quantification or categorization of organ deformation is not easy. However, correction of the setup error according to prostate motion by use of a 6 degrees-of-freedom couch might minimize the impact of deformation.

5. CONCLUSION

The mean value of the maximum dose differences between the original VMAT plan and the tilted one was about only 3%. The value of the HI for the PTV had an increasing trend according to the pitch angle error, and the values of the D_{95} for the PTV and D_{2ml}, V_{50}, V_{60}, and V_{70} for the rectum had decreasing trends. However, there was no correlation between these indexes and the maximum dose difference. Body leaning caused by the pitch angle error correction had little effect on the dose distribution; in contrast, the pitch angle correction can reduce the effects of organ displacement and improve the dose and volume indexes. Thus, the pitch angle setup error in VMAT for prostate cancer should be corrected with the pitch angle error of the prostate.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

REFERENCES

1. Schallenkamp JM, Herman MG, Kruse JJ et al. Prostate position relative to pelvic bony anatomy based on intraprostatic gold markers and electronic portal imaging. Int J Radiat Oncol Biol Phys 2005;63(3):800-11.
2. Ghilezan MJ, Jaffray DA, Siewerdsen JH et al. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). Int J Radiat Oncol Biol Phys

2005;62(2):406-17.

3. Barney BM, Lee RJ, Handrahan D et al. Image-guided radiotherapy (IGRT) for prostate cancer comparing kV imaging of fiducial markers with cone beam computed tomography (CBCT). Int J Radiat Oncol Biol Phys 2011;80(1):301-5.
4. Byrne TE. A review of prostate motion with considerations for the treatment of prostate cancer. Med Dosim 2005;30(3):155-61.
5. Graf R, Wust P, Budach V et al. Potentials of on-line repositioning based on implanted fiducial markers and electronic portal imaging in prostate cancer radiotherapy. Radiat Oncol 2009;4:13.
6. Ikeda I, Mizowaki T, Sawada Y et al. Assessment of inter-fractional prostate motion in patients immobilized in the prone position using a thermoplastic shell. J Radiat Res 2014;55(1):168-74.
7. Owen R, Kron T, Foroudi F et al. Interfraction prostate rotation determined from in-room computerized tomography images. Med Dosim 2011;36(2):188-94.
8. Hoogeman MS, van Herk M, de Bois J et al. Strategies to reduce the systematic error due to tumor and rectum motion in radiotherapy of prostate cancer. Radiother Oncol 2005;74(2):177-85.
9. Takemura A, Shoji S, Ueda S et al. Effect of daily setup errors on individual dose distribution in conventional radiotherapy: an initial study. Radiol Phys Technol 2009;2(2):151-8.
10. Fu W, Yang Y, Yue NJ et al. Dosimetric influences of rotational setup errors on head and neck carcinoma intensity-modulated radiation therapy treatments. Med Dosim 2013;38(2):125-32.
11. Cranmer-Sargison G. A treatment planning investigation into the dosimetric effects of systematic prostate patient rotational set-up errors. Med Dosim 2008;33(3):199-205.

12. Yokoi T, Ueda S, Takemura A et al. Development of a New Simulation Method of Dose-Distribution Changes for an IMRT Plan by Rotational Setup Error. Int J Radiat Oncol Biol Phys 2012: 84(3S): S774-S775.
13. Zhang Q, Xiong W, Chan MF et al. Rotation effects on the target-volume margin determination. Physica medica 2015:31(1): 80-84.
14. McNair HA, Hansen VN, Parker CC et al. A comparison of the use of bony anatomy and internal markers for offline verification and an evaluation of the potential benefit of online and offline verification protocols for prostate radiotherapy. Int J Radiat Oncol Biol Phys 2008;71(1):41-50.
15. International Commission on Radiation Units and Measurements. Report 83: Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT). Journal of the ICRU 2010: 10(1), 1-106.
16. Wognum S, Heethuis SE, Rosario T et al. Validation of deformable image registration algorithms on CT images of ex vivo porcine bladders with fiducial markers. Medical Physics 2014; 41(7): 071916.
17. Luu C, Goldstein L, Goldner B et al. Trends in radiotherapy after breast-conserving surgery in elderly patients with early-stage breast cancer. Annals of surgical oncology 2013; 20(10): 3266-73.
18. Amin MB, Angeles L, Bruner DW et al. A phase III randomized study of hypofractionated 3D-CRT/IMRT versus conventionally fractionated 3D-CRT/IMRT in patients with favorable-risk prostate cancer. RTOG 0415. http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?action=openFile&FileID=4624 Accessed 9 May 2014.
19. Fiorino C, Sanguineti G, Cozzarini C et al. Rectal dose-volume constraints in high-dose radiotherapy of localized prostate cancer. Int J Radiat Oncol 2003;57(4):953-62.

FIGURE LEGENDS

Fig. 1. Illustration showing pitch angle directions.

Fig. 2. CT image set with a virtual pitch angle error. The original position of the body is indicated by dashed lines in slices a and c. The body in the images was shifted by the distances d_1 and d_2; they depend on the angle θ and the distance from a slice that includes the isocenter.

Fig. 3 Dose indexes for CTV

Circles in the graphs show the values for the case in each index, boxes indicate the range of the standard deviation for the values, and bars represent the maximum and minimum values. All of the dose indexes had no significance by the Kruskal–Wallis test and the Jonckheere–Terpstra test.

Fig. 4 Dose indexes for PTV

Circles in the graphs show the values for the cases, boxes indicate the range of the standard deviation for the values, and bars represent the maximum and minimum values. All of the dose and volume indexes had no significant difference by the Kruskal–Wallis test, but the D_{95} and the HI had significant trends as tested by the Jonckheere–Terpstra test ($p<0.05$).

Fig. 5 Dose and volume indexes for bladder

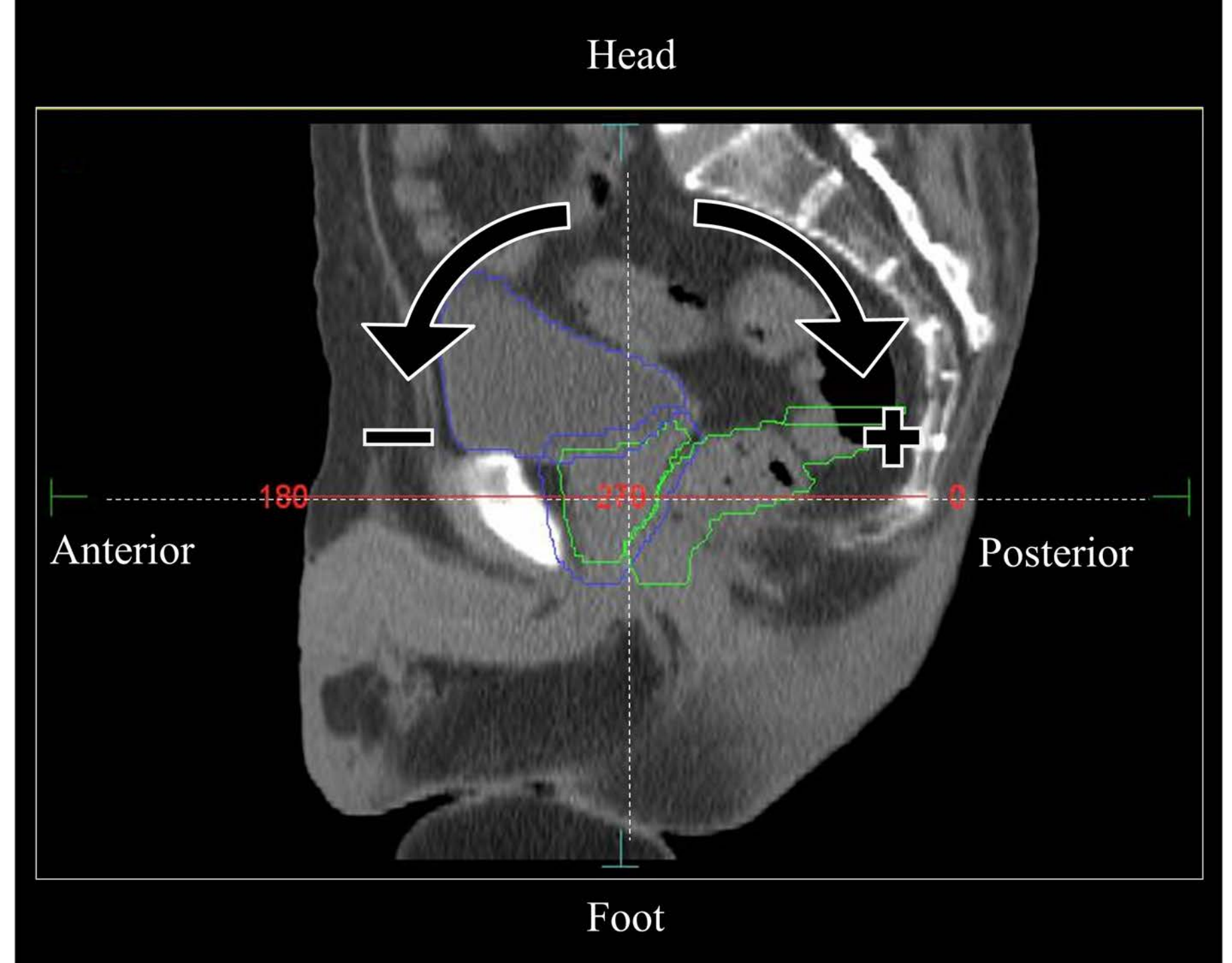
Circles in the graphs show the values for the cases in each index, boxes indicate the range of the standard deviation for the values, and bars represent the maximum and minimum values. All of the dose and volume indexes had no significance by the Kruskal–Wallis test and the Jonckheere–Terpstra test.

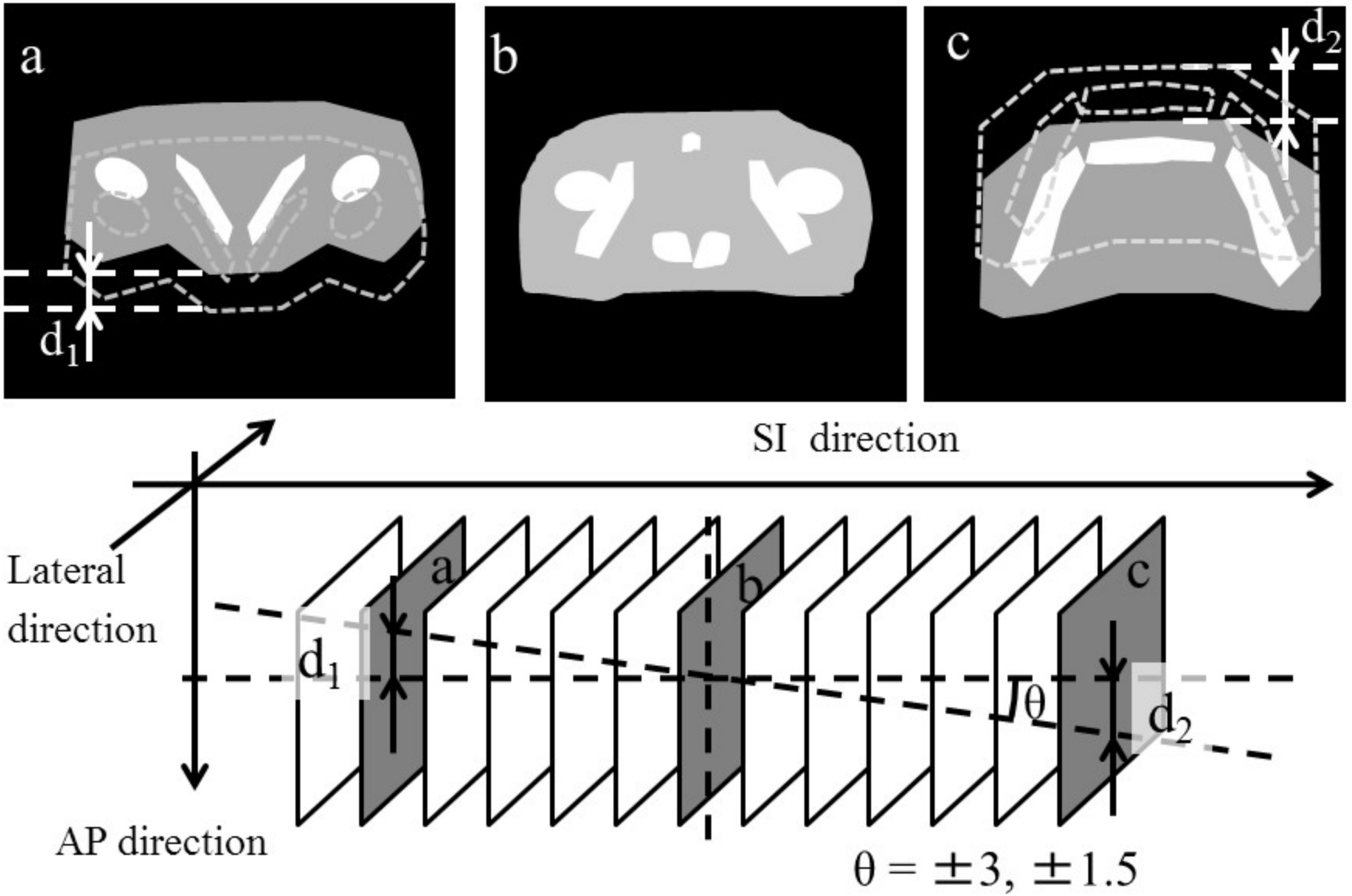
Fig. 6 Dose and volume indexes for rectum

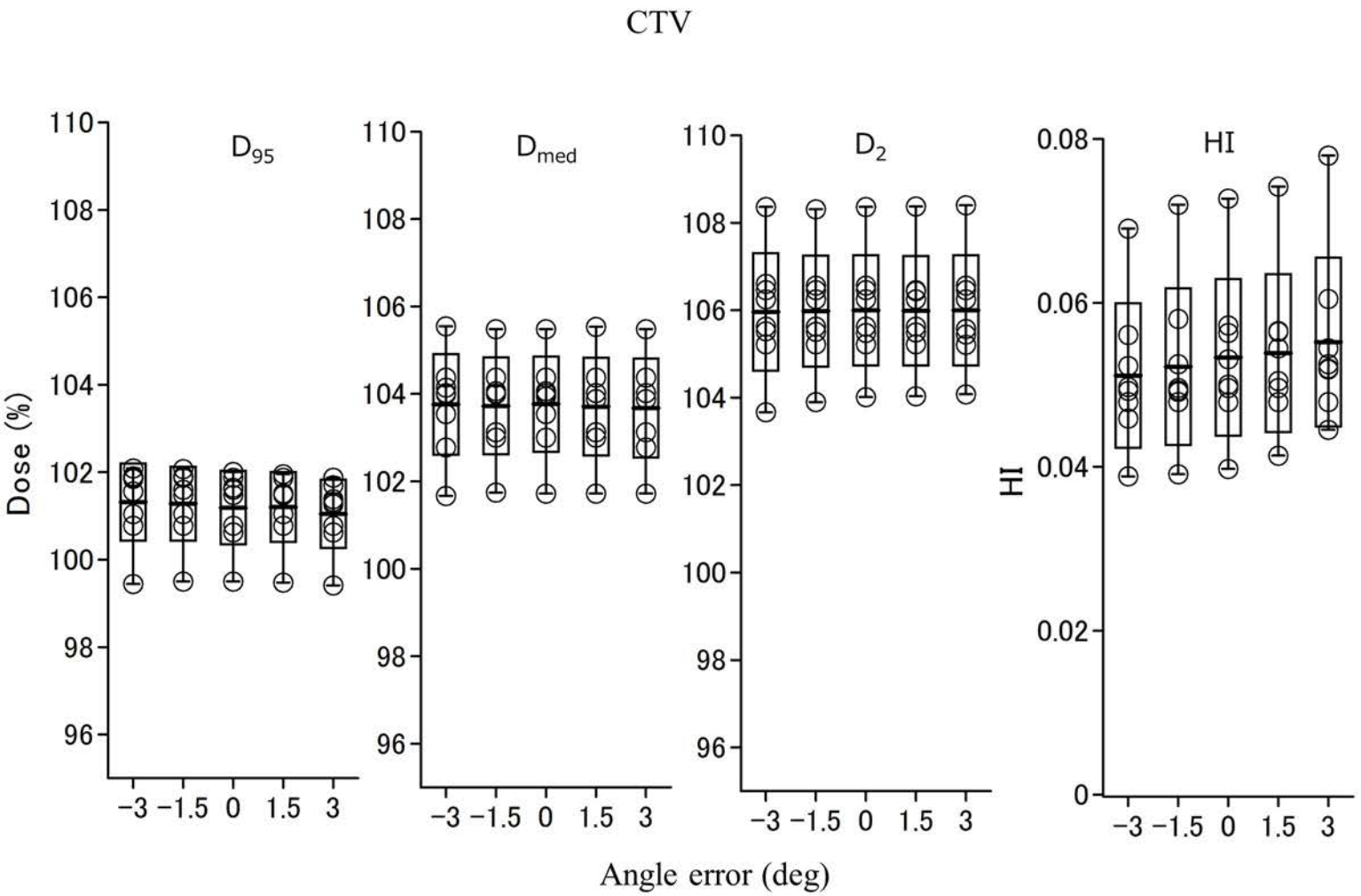
Circles in the graphs show the valuse for the cases in each index, boxes indicate the range of the standard deviation for the values, and bars represent the maximum and minimum values. All of the dose and volume indexes had no significant difference by the Kruskal–Wallis test, but the D_{2ml}, V_{50}, the V_{60}, and the V_{70} had significant trends as tested by the Jonckheere–Terpstra test ($p<0.05$).

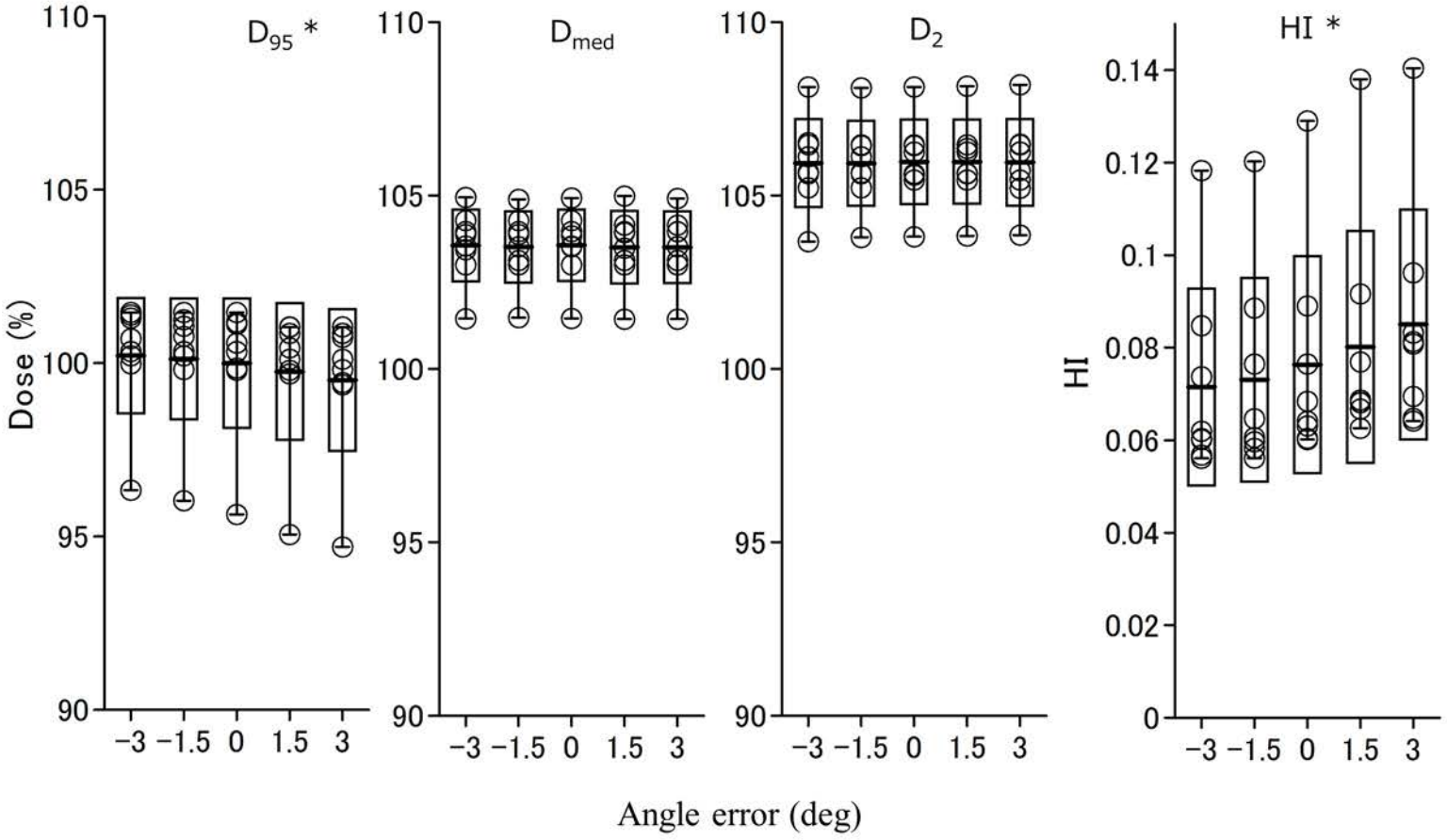
Fig. 7. Example of subtracted dose overlaying on the CT image. The dose differences between the dose distributions on the original plan and the -3 degrees tilted one are shown. This case has the largest value of the maximum dose difference (5.62%; white arrow) of all the cases, and the location of the largest difference is around the PTV (white triangles). The anterior and posterior skin areas (top and bottom of the body in the CT image) represent large differences between the dose to tissue and the dose to air because of the body tilt. The skin area was excluded from the calculation of the maximum dose difference in the CT images.

Fig. 8. Graphs showing the correlation between the maximum dose difference, and the dose and volume indexes whose values were dependent on the pitch angle. Graph (a) shows the correlation between the maximum dose difference and the absolute value of the PTV ΔD_{95}. Graph (b) shows the correlation between the maximum dose difference and the absolute value of the PTV ΔHI. Graph (c) shows the correlation between the maximum dose difference and the absolute value of the ΔD_{2ml} for the rectum. Graph (d) shows the correlation between the maximum dose difference and absolute value of the ΔV_{50}, ΔV_{60}, ΔV_{70} for the rectum.

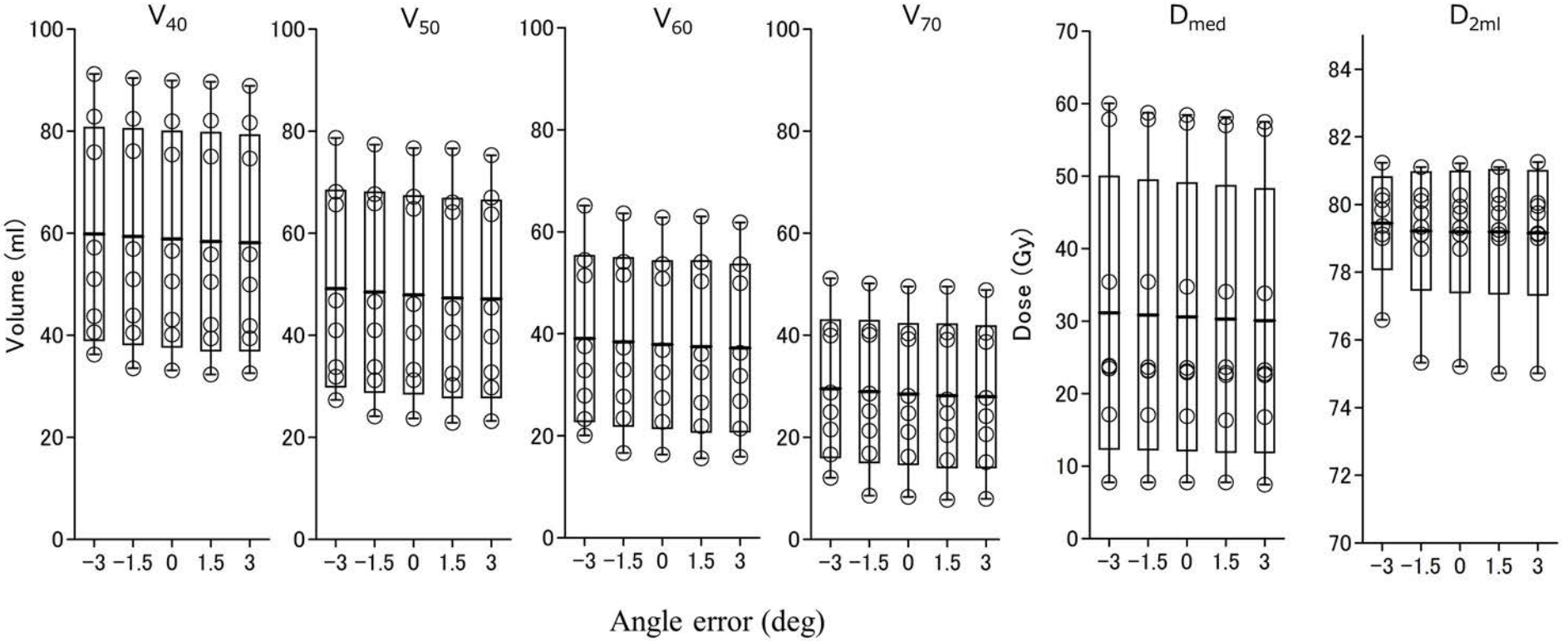

Head
180
270
0
Anterior
Posterior
Foot

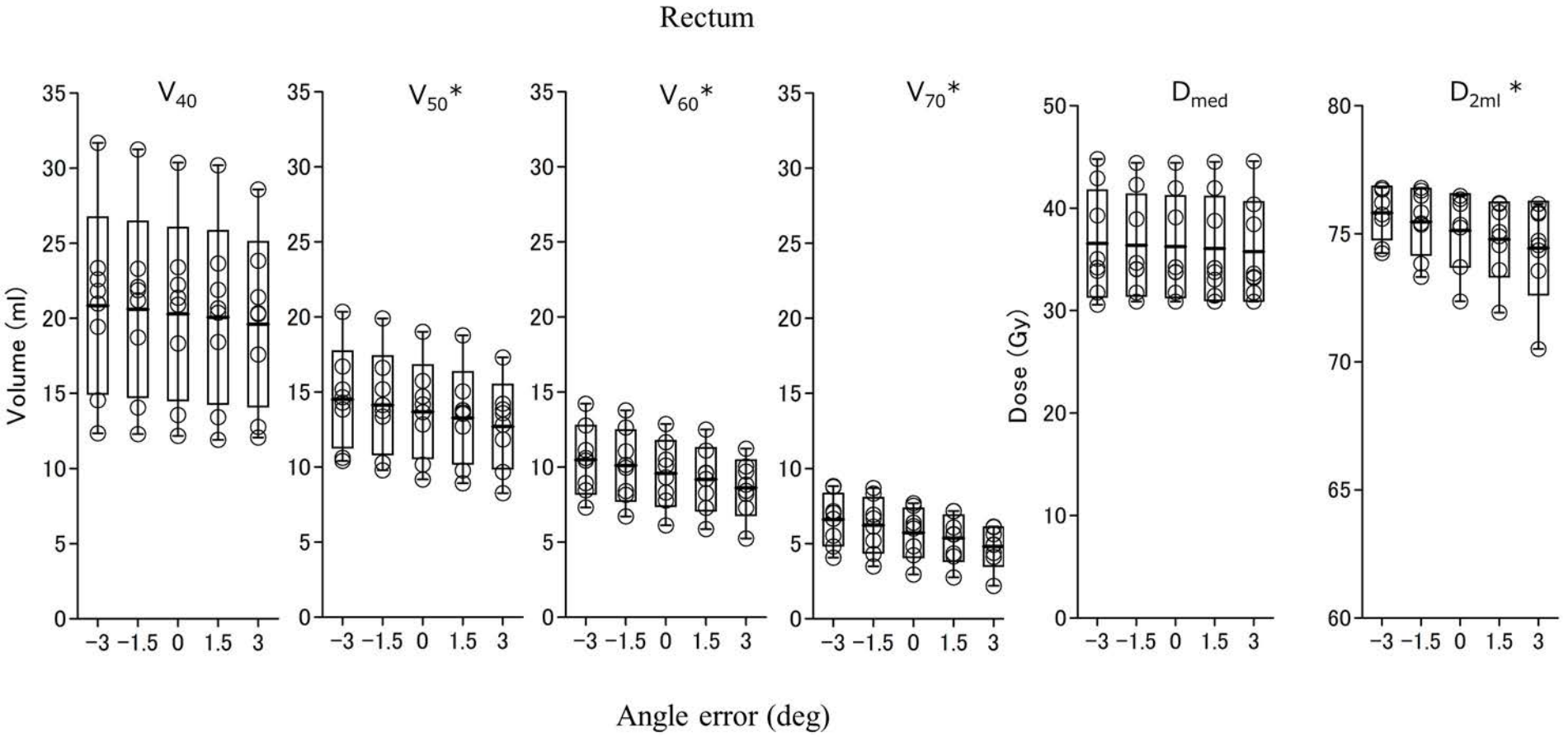

a
b
c
d_1
d_2
SI direction
Lateral direction
AP direction
θ
$\theta = \pm 3, \pm 1.5$


CTV
D95
Dmed
D2
HI
Dose (%)
HI
110
108
106
104
102
100
98
96
0.08
0.06
0.04
0.02
0
−3 −1.5 0 1.5 3
Angle error (deg)

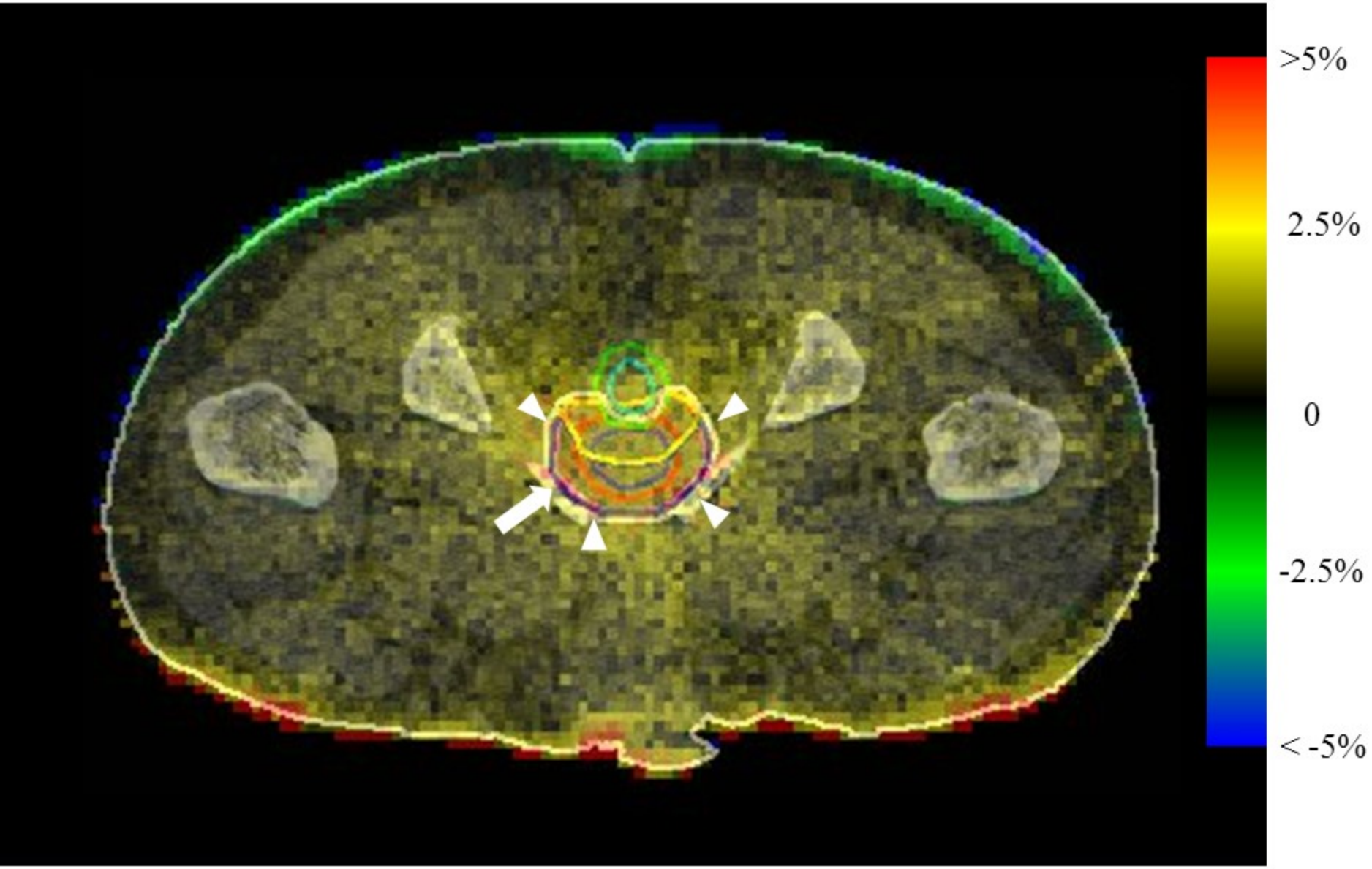


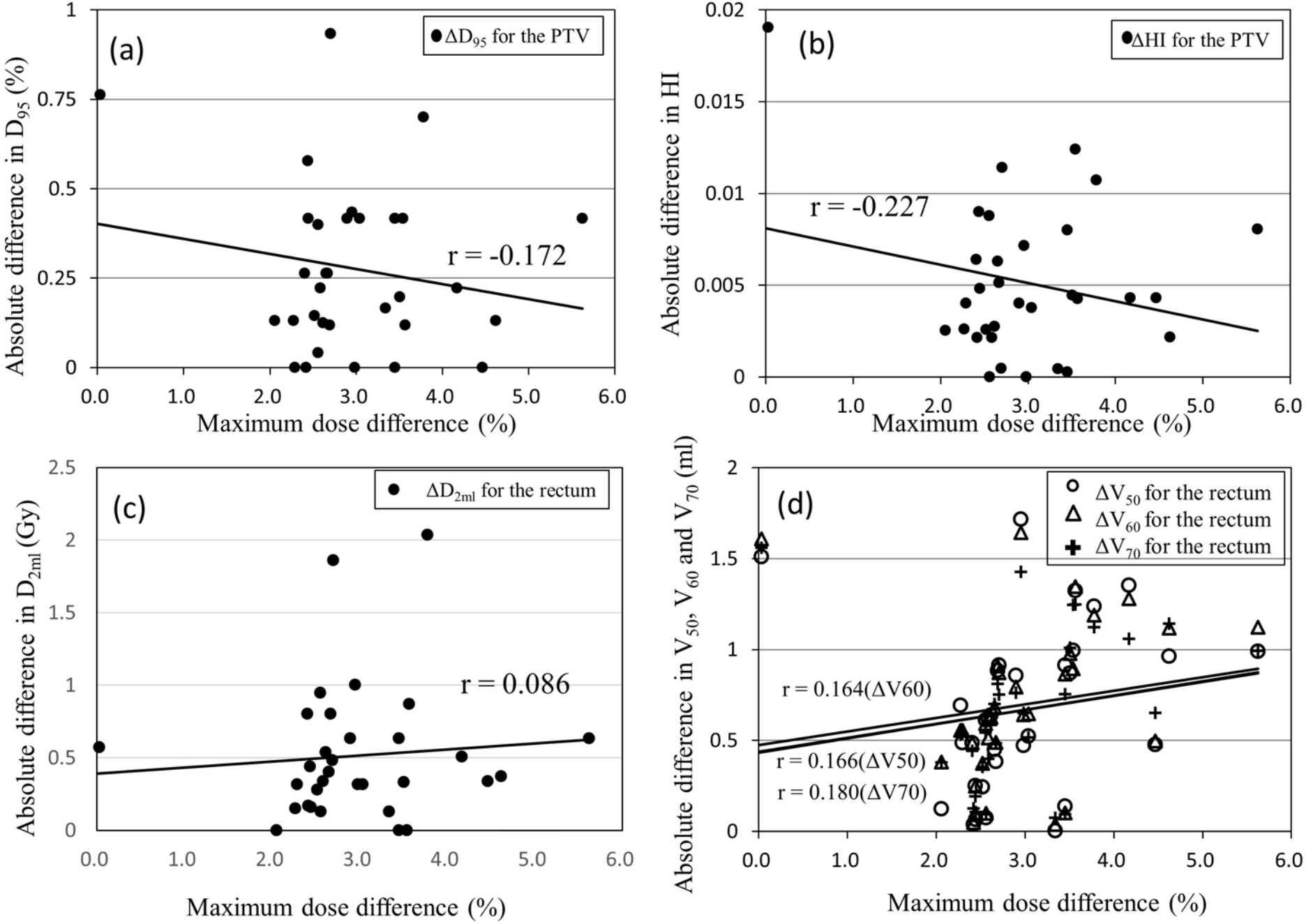
* Significant by the Jonckheere-Terpstra test ($p < 0.05$)


Bladder
V40
V50
V60
V70
Dmed
D2ml
Volume (ml)
Dose (Gy)
Angle error (deg)
−3 −1.5 0 1.5 3



* Significant by the Jonckheere-Terpstra test ($p < 0.05$)


>5%
2.5%
0
-2.5%
< -5%


(a)
ΔD95 for the PTV
Absolute difference in D95 (%)
r = -0.172
Maximum dose difference (%)
(b)
ΔHI for the PTV
Absolute difference in HI
r = -0.227
Maximum dose difference (%)
(c)
ΔD2ml for the rectum
Absolute difference in D2ml (Gy)
r = 0.086
Maximum dose difference (%)
(d)
ΔV50 for the rectum
ΔV60 for the rectum
ΔV70 for the rectum
Absolute difference in V50, V60 and V70 (ml)
r = 0.164(ΔV60)
r = 0.166(ΔV50)
r = 0.180(ΔV70)
Maximum dose difference (%)