Published in final edited form as:

Phys Med Biol. ; 64(8): 085016. doi:10.1088/1361-6560/ab10a0.

An atlas-based method to predict three-dimensional dose distributions for cancer patients who receive radiotherapy

SA Yoganathan¹ and Rui Zhang^{1,2,a}

¹Physics and Astronomy, Louisiana State University, Baton Rouge, LA70803

²Radiation Oncology, Mary Bird Perkins Cancer Center, Baton Rouge, LA70809

Abstract

Due to the complexity of advanced radiotherapy techniques, the treatment planning process is usually time consuming and the plan quality can vary considerably among planners and institutions. It is also impractical to generate all possible treatment plans based on available radiotherapy techniques and select the best option for a specific patient. Automatic dose prediction will be very helpful in these situations, while there were a few studies of three-dimensional (3D) dose prediction for patients who received radiotherapy. The purpose of this work was to develop a novel atlas-based method to predict 3D dose prediction and to evaluate its performance. Previously treated nineteen left-sided post-mastectomy breast cancer patients and sixteen prostate cancer patients were included in this study. One patient was arbitrarily chosen as the reference for each type of cancer and all the remaining patients' computed tomography (CT) images and contours were aligned to it using deformable image registration (DIR). Deformable vector field (DVF) for each patient i (DVF_{i-ref}) was used to deform the original 3D dose matrix of that patient. CT scan of the test patient was also registered with the same reference patient using DIR and both direct DVF ($DVF_{test-ref}$) and inverse DVF ($DVF_{test-ref}^{-1}$) were derived. Similarity of atlas patients to the test patient was determined based on the similarity of $DVF_{test-ref}$ to atlas DVFs (DVF_{i-ref}) and appropriate weighting factors were calculated. Patients' doses in the atlas were deformed again using $DVF_{test-ref}^{-1}$ to transform them from the reference patient's coordinates to the test patient's coordinates and the final 3D dose distribution for the test patient was predicted by summing the weighted individual 3D dose distributions. Performance of our method was evaluated and the results revealed that the proposed method was able to predict the 3D dose distributions accurately. The mean dose difference between clinical and predicted 3D dose distributions were 0.9 ± 1.1 Gy and 1.9 ± 1.2 Gy for breast and prostate plans. The proposed dose prediction method can be used to improve planning quality and facilitate plan comparisons.

Keywords

atlas-based; dose prediction; deformable image registration; radiotherapy

^a Corresponding author: Rui Zhang, Department of Physics and Astronomy, Louisiana State University, Baton Rouge, LA, USA. Phone: 225-215-1132; rzhang@lsu.edu.

Conflict of interest statement

The authors have no conflicts of interest.

1. Introduction

The role of radiotherapy in cancer care is evolving rapidly with the adoption of new technologies. The more advanced ones like intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) have the potential to improve treatment quality by constraining therapeutic doses to radiosensitive organs. However, the high dose modulation increases the complexity of treatment plans, and inverse planning is usually iterative and time consuming. The quality of treatment plans would also vary considerably among different planners and institutions (Das *et al.*, 2008; Nelms *et al.*, 2012; Batumalai *et al.*, 2013), which means sub-optimal treatment plans may be produced (Wu *et al.*, 2009; Moore *et al.*, 2011) and may compromise patient care (Moore *et al.*, 2015). An optimal treatment plan for a specific patient depends on many factors and it is very challenging to recommend a certain modality to the patient. Physicians usually make decisions based on experience, while theoretically the planner should generate plans based on all available radiotherapy techniques to find the best option for a patient, which is laborious and impractical.

Automatic dose prediction methods were proposed to reduce the planning time and improve the plan quality. They can also be used to predict the dose distributions of different radiotherapy techniques and facilitate plan selection. These methods could be grouped into two main categories: one-dimensional (1D) and three-dimensional (3D) methods. The 1D methods predict the dose volume histogram (DVH) data based on previous patient plans and estimate target DVH objectives for new plan optimizations (Wu *et al.*, 2011; Shiraishi *et al.*, 2015). These methods have limited spatial information and may constrain users' capability to control final dose distributions. The 3D methods predict dose on a voxel-by-voxel basis. Shiraishi and Moore (2016) demonstrated a 3D dose prediction model using an artificial neural network and tested applicability of their model using prostate and stereotactic radiosurgery/radiotherapy (SRS/SRT) patients. Their model included only the voxels within 30 mm of prostate planning target volume (PTV) edge and 32 mm of SRS/SRT PTV edge. McIntosh and Purdie (2017) reported a multiple-atlas-based dose prediction approach and they evaluated their model for six treatment sites. Deformable image registration was used for the comparison with their proposed dose prediction method (contextual atlas regression forests) on atlas-dose to novel image mapping. In a separate paper, McIntosh *et al.* (2017) also converted the predicted dose distributions to complete treatment plans using voxel-based dose mimicking optimization. Chen *et al.* (2019) used residual neural network-based deep learning approach to generate 3D dose distribution for step-and-shoot IMRT of early-stage nasopharyngeal cancer patients. Structure images were used as the input while the information from CT images was not considered in their study. They found including the radiation beam geometry like distance to field boundary improved the prediction accuracy. Fan *et al.* (2019) also reported a model using residual neural network-based deep learning. In addition to 3D dose prediction for head-and-neck patient treated with step-and-shoot IMRT, they converted the predicted doses to clinically acceptable plans by adopting a simple objective function. Mahmood *et al.* (2018) reported a 3D dose prediction method based on generative adversarial network, and they also converted predicted dose distributions to optimized plans through inverse optimization.

The atlas-based approach is commonly used in medical field for automatic segmentation (Sharp *et al.*, 2014), and the contours of a novel patient are automatically transferred from the previously contoured atlases based on the optimal non-linear registration. Similarly, the atlas-based approach can also be used to transfer the 3D dose distributions from the previously planned dose files (atlases) to a novel patient (McIntosh and Purdie, 2017), but such methods have not been extensively investigated. The purpose of this work was to develop a simple and novel atlas-based 3D dose prediction method for radiotherapy and evaluate its performance for breast and prostate cancer patients.

2. Methods and materials

2.1. Patient selection

Previously treated nineteen left-sided post-mastectomy breast cancer and sixteen prostate cancer patients were included in this study. CT scans were acquired using a wide bore 16 slice CT scanner with 2.5mm slice thickness. All the breast patients were planned for a total dose of 50Gy in 25 fractions using two coplanar 6 MV volumetric modulated arc therapy (VMAT) arcs. The prostate patients were planned using two coplanar 6 MV VMAT arcs and prescription doses were in the range of 45–76Gy delivered in 25–38 fractions. To unify the data, all the prostate plans were normalized to deliver 70Gy (35 fractions) to 100% PTV volume. All the plans were created in a commercial treatment planning system (TPS) (Pinnacle³, version 9.8, Philips Medical Systems, Fitchburg, WI). The DICOM files of each patient including CT images, organ contours and 3D dose matrix were exported from the TPS and anonymized (Newhauser *et al.*, 2014) for this study.

2.2 Atlas construction

The workflow of atlas construction is shown in figure 1 (within dashed lines). One patient was arbitrarily chosen as the reference, and all the remaining patients' CT and contours were registered with the reference patient using deformable image registration (DIR). The open-source software named deformable image registration and adaptive radiotherapy (DIRART) toolkit was used (Yang *et al.*, 2011). During the registration process (Horn-Schunck optical flow algorithm with default four resolution phase parameters), it is necessary to ensure proper matching of contours between any atlas patient and the reference patient. Deformable vector field (DVF) for each patient i derived from the above registration (DVF_{i-ref}) will be used to deform the original 3D dose matrix of that patient. This process was repeated for all the patients and finally an atlas of DVFs and deformed doses ($Dose_{i-ref}$) (aligned to the reference patient) was generated (breast cancer atlas contained eighteen patients and prostate cancer atlas contained fifteen patients because one patient in each group was chosen as the reference and was not included in the atlas).

2.3 Dose prediction

Figure 1 also shows the workflow of dose prediction for a test patient for which the dose is to be predicted. CT scan of the test patient was registered with the reference patient and both direct DVF ($DVF_{test-Ref}$) and inverse DVF ($DVF_{test-Ref}^{-1}$) were derived. Similarity of atlas patients to the test patient was determined using DVFs based on the assumption that two patients have similar anatomy if they have similar DVFs when they are aligned to the same

reference patient, and similarity of $DVF_{\text{test-Ref}}$ to atlas DVFs ($DVF_{i\text{-Ref}}$) was measured using structural similarity index (SSIM) (Wang *et al.*, 2004). The SSIM measures the similarity of two images and is calculated using the following formula:

$$SSIM = \frac{(2\mu_i\mu_{test} + c_1)(2\sigma_{i,test} + c_2)}{(\mu_i^2 + \mu_{test}^2 + c_1)(\sigma_i^2 + \sigma_{test}^2 + c_2)}, \quad (1)$$

Where μ_i and μ_{test} are the local means calculated over a 2D slice of $DVF_{i\text{-Ref}}$ and $DVF_{\text{test-Ref}}$, σ_i and σ_{test} are the local standard deviation calculated over a 2D slice of $DVF_{i\text{-Ref}}$ and $DVF_{\text{test-Ref}}$, $\sigma_{i,test}$ is the cross co-variance of two images, C_1 and C_2 are regularization constants and are used to ensure stability when the denominator approaches zero, i.e. μ or σ is close to zero. The SSIM value was calculated for each CT slice, and the mean SSIM index (MSSIM) of all slices was calculated as follows

$$MSSIM = \frac{\sum_{i=1}^m SSIM_i}{m}, \quad (2)$$

where m is the number of CT slices for a patient. A weighting factor (W_i) was determined for patient i in the atlas based on the MSSIM index, i.e. a higher value of W_i is assigned to a patient with higher MSSIM index and vice-versa. Patients' doses in the atlas will be deformed again using $DVF_{\text{test-ref}}^{-1}$ to transform them from the reference patient's coordinates to the test patient's coordinates and are multiplied by the respective W_i . The final 3D dose distribution for the test patient will be predicted by summing the weighted individual 3D dose distributions:

$$D(\text{test}) = \sum_{i=1}^n W_i \times D_i, \quad (3)$$

where n is the total number of patients in the atlas.

2.4 Model validation

Performance of the dose prediction model was evaluated using “leave-one-out cross validation” approach. In this method, $n-1$ patients (training) were used to train the model and the dose distribution was predicted for the one remaining patient (validation), and this procedure is repeated for all possible combinations of training and validation data. The predicted doses were compared with the original clinical doses: PTV coverage was evaluated using $D_{95\%}$ (dose to 95% of PTV volume); for breast patients, the organs at risk (OAR) considered were heart ($V_{22.5}$), total lungs (left and right combined) (V_{20}), contralateral breast (V_5) and spinal cord (D_{max}); for prostate patients, the OARs considered were rectum (V_{50}), bladder (V_{65}) and right-left femoral head (V_{50}). The parameters in the parenthesis represent the volume of OAR receiving a particular dose value or more.

2.5 Impact of atlas size

In order to test the impact of total number of patients in the atlas on the accuracy of dose prediction, the model was trained with different number of breast cancer patients (2, 5, 10 and 17), and the impact of atlas size was evaluated for five other breast cancer patients.

3. Results

Figure 2 shows dose volume histogram (DVH) comparisons for typical breast patients (7 and 14) and prostate patients (4 and 5): solid lines represent clinical DVH and dashed lines represent predicted DVH. Figure 3 shows dose distribution comparison for breast cancer patients 7 and 14 and prostate cancer patients 4 and 5. The main reasons for larger dose deviations in breast patient 14 and prostate patient 5 are the inefficiency of registration algorithms at high dose gradient regions (near skin surfaces) and the slightly atypical anatomy of those patients.

Prediction accuracy of the model was analyzed. Average DVH parameters for all breast and prostate patients are shown in figure 4. The PTV coverage was very close between predicted and clinical plans, while OARs doses were overall lower in predicted plans. Figure 5 shows the mean absolute dose difference (over entire CT volume) for all patients ($D = |D_{clin} - D_{pred}|$) and the average dose difference was observed to be 0.9 ± 1.1 Gy for breast plans and 1.9 ± 1.2 Gy for prostate plans.

The impact of atlas size on the performance of dose prediction was also evaluated. Figure 6 shows the DVH of predicted plans for a typical breast cancer patient using various atlas sizes. PTV coverage was very similar for all atlas sizes, but OAR doses were improved with increased sample size. These were also demonstrated in Table 1 which shows the comparison of mean DVH parameters (average values of 5 patients) based on various atlas sizes.

The atlas model generation takes approximately 90 minutes for breast (18 patients) and 75 minutes for prostate (15 patients) on a 2.5 GHz Intel i5 processor with 8 GB random-access memory (Intel Corp., Santa Clara, CA), and the model generation is required only once. Dose prediction for a new patient takes approximately 10 minutes (5 minutes for DIR and 5 minutes for dose prediction).

4. Discussion

In this study, a simple and novel method was developed to predict 3D radiotherapy dose distributions for cancer patients using weighted summation of deformed atlas doses. The mean absolute dose difference between clinical and predicted 3D dose distributions were 0.9 ± 1.1 Gy and 1.9 ± 1.2 Gy for breast and prostate plans. Our method can be used to help the planners generate treatment plans with consistent quality and guide automated planning. It can also facilitate faster dose evaluation and ranking of possible RT techniques, narrow down the possible choices, and help clinical decision-making.

Compared with traditional atlas-based methods, our method only requires DIRs between the reference patient and remaining atlas patients once and for all, and DIR between the new

patient and the reference patient, while does not need DIR between the new patient and remaining atlas patients. Our dose prediction takes around 10 minutes for a new patient, which is comparable with 15 minutes run-time previously reported by McIntosh and Purdie (2017). DIRART toolkit was also used by McIntosh and Purdie (2016, 2017) for the comparison with their proposed dose prediction method (contextual atlas regression forests) on atlas-dose to novel image mapping, while DIRART was the essential tool for image deformation, generation of weighting factors and dose mapping in our study.

The general findings of our work are consistent with literature. Shiraishi and Moore (2016) showed that the average prediction error was less than 10% for prostate VMAT, and our result shows $2.8 \pm 2.9\%$ for prostate VMAT. McIntosh and Purdie (2017) used the mean absolute difference (MAD), which is the mean difference between clinical and predicted DVHs averaged over all region of interest, to compare the clinical and predicted DVHs. Their reported MAD values were $0.64 \pm 0.43\%$ and $2.13 \pm 0.75\%$ for breast and prostate patients. We also calculated the MAD values and they are $0.2 \pm 3.2\%$ and $0.7 \pm 1.9\%$ for breast and prostate patients.

It is found that PTV coverage in predicted plans does not change significantly with number of patients used in the atlas, but OAR sparing in predicted plans improves with atlas size. The current study included limited number of patients and only evaluated two disease sites, while the next phase of our study will involve various sites with larger datasets. As pointed out in the literature, atlas selection plays an important role in atlas-based techniques. Aljabar *et al.* (2009) reported that selecting atlases based on image similarity and demographic information (age) could improve the accuracy of atlas-based brain segmentation. Sanroma *et al.* (2014) used a learning-based approach to select the best atlases for multiple-atlas segmentation. McIntosh and Purdie (2016, 2017) used atlas regression forests to select the most effective atlases for dose prediction. Unlike these work, our study uses weighted average of atlases and includes only a relatively small sample size, which is one of the limitations of our study. As our library size is relatively small, we chose to use all the atlases with appropriate weighting factors which were determined based on SSIM between the atlas patient and the novel patient. The impact of atlas selection on our method would be interesting to investigate when a large sample sizes is used.

The current study shows that the OAR doses of some patients are better spared in predicted plans, so the future study should investigate the quantity of benefit from dose prediction. McIntosh and Purdie (2017) pointed out predicted OAR sparing or better target coverage may not actually be achievable for the real treatment, whereas Shiraishi and Moore (2016) suggested predicted dose distributions are deliverable because they are generated based on deliverable plans. Other studies (McIntosh *et al.*, 2017; Mahmood *et al.*, 2018; Fan *et al.*, 2019) showed that predicted 3D dose distributions can be converted to clinically acceptable plans by adopting certain objective functions. As artificial intelligence techniques continue to improve, it is anticipated the predicted plans will be closer and closer to deliverable plans, but inverse planning will still be required in the dose conversion process and more exploration in this direction is needed.

Our DIR based method performs well on fixed anatomy like chest wall, whole breast and prostate, whereas it may not be well suited for the freely moving anatomy like lung, breast cavity etc., as previously discussed by McIntosh and Purdie (2017). A separate study is needed to quantify the performance of our atlas method on these sites. The other possible problem is that predicted patient dose may be different from clinical dose distribution for a new patient with atypical anatomy. As shown in this study, the mean whole body dose difference between predicted and clinical doses was low for the nineteen breast cancer and sixteen prostate cancer patients we evaluated, so it is reasonable to expect small dose discrepancy for most patients. We will continue to include more patients into our atlases, predict doses, and look out for errors. To use our method for a new patient (no existing plan) with very atypical anatomy like really obese or thin, we suggest creating one or two plans for him or her according to clinical protocols, and comparing these plans with predicted plans. If dose discrepancy is large, it will be prudent to create all possible plans for the patient and include him or her in a special patient atlas.

5. Conclusion

This study describes a simple and novel method to predict 3D dose distributions using weighted summation of deformed atlas doses. Performance of the dose prediction model was evaluated for breast and prostate cancer patients. Most of the predicted plans were comparable to clinical plans. Our method can be used to improve planning quality and facilitate plan comparisons.

Acknowledgements

This work was partially supported by National Institutes of Health (grant no. K22CA204464).

References

- Aljabar P, Heckemann RA, Hammers A, Hajnal JV and Rueckert D 2009 Multi-atlas based segmentation of brain images: atlas selection and its effect on accuracy *NeuroImage* 46 726–38 [PubMed: 19245840]
- Batumalai V, Jameson MG, Forstner DF, Vial P and Holloway LC 2013 How important is dosimetrist experience for intensity modulated radiation therapy? A comparative analysis of a head and neck case *Practical radiation oncology* 3 e99–e106 [PubMed: 24674377]
- Chen X, Men K, Li Y, Yi J and Dai J 2019 A feasibility study on an automated method to generate patient-specific dose distributions for radiotherapy using deep learning *Med Phys* 46 56–64 [PubMed: 30367492]
- Das JJ, Cheng CW, Chopra KL, Mitra RK, Srivastava SP and Glatstein E 2008 Intensity-modulated radiation therapy dose prescription, recording, and delivery: patterns of variability among institutions and treatment planning systems *J Natl Cancer Inst* 100 300–7 [PubMed: 18314476]
- Fan J, Wang J, Chen Z, Hu C, Zhang Z and Hu W 2019 Automatic treatment planning based on three-dimensional dose distribution predicted from deep learning technique *Med Phys* 46 370–81 [PubMed: 30383300]
- Mahmood R, Babier A, McNiven A, Diamant A and Chan TCY 2018 Automated treatment planning in radiation therapy using generative adversarial networks *Proceedings of Machine Learning Research* 85 1–14
- McIntosh C and Purdie TG 2016 Contextual Atlas Regression Forests: Multiple-Atlas-Based Automated Dose Prediction in Radiation Therapy *IEEE transactions on medical imaging* 35 1000–12 [PubMed: 26660888]

- McIntosh C and Purdie TG 2017 Voxel-based dose prediction with multi-patient atlas selection for automated radiotherapy treatment planning *Phys Med Biol* 62 415–31 [PubMed: 27997376]
- McIntosh C, Welch M, McNiven A, Jaffray DA and Purdie TG 2017 Fully automated treatment planning for head and neck radiotherapy using a voxel-based dose prediction and dose mimicking method *Phys Med Biol* 62 5926–44 [PubMed: 28486217]
- Moore KL, Brame RS, Low DA and Mutic S 2011 Experience-based quality control of clinical intensity-modulated radiotherapy planning *Int J Radiat Oncol Biol Phys* 81 545–51 [PubMed: 21277097]
- Moore KL, Schmidt R, Moiseenko V, Olsen LA, Tan J, Xiao Y, Galvin J, Pugh S, Seider MJ, Dicker AP, Bosch W, Michalski J and Mutic S 2015 Quantifying Unnecessary Normal Tissue Complication Risks due to Suboptimal Planning: A Secondary Study of RTOG 0126 *Int J Radiat Oncol Biol Phys* 92 228–35 [PubMed: 25847605]
- Nelms BE, Robinson G, Markham J, Velasco K, Boyd S, Narayan S, Wheeler J and Sobczak ML 2012 Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems *Practical radiation oncology* 2 296–305 [PubMed: 24674168]
- Newhauser W, Jones T, Swerdloff S, Newhauser W, Cilia M, Carver R, Halloran A and Zhang R 2014 Anonymization of DICOM electronic medical records for radiation therapy *Computers in biology and medicine* 53 134–40 [PubMed: 25147130]
- Sanroma G, Wu G, Gao Y and Shen D 2014 Learning to rank atlases for multiple-atlas segmentation *IEEE transactions on medical imaging* 33 1939–53 [PubMed: 24893367]
- Sharp G, Fritscher KD, Pekar V, Peroni M, Shusharina N, Veeraraghavan H and Yang J 2014 Vision 20/20: perspectives on automated image segmentation for radiotherapy *Med Phys* 41 050902 [PubMed: 24784366]
- Shiraishi S and Moore KL 2016 Knowledge-based prediction of three-dimensional dose distributions for external beam radiotherapy *Med Phys* 43 378 [PubMed: 26745931]
- Shiraishi S, Tan J, Olsen LA and Moore KL 2015 Knowledge-based prediction of plan quality metrics in intracranial stereotactic radiosurgery *Med Phys* 42 908 [PubMed: 25652503]
- Wang Z, Bovik AC, Sheikh HR and Simoncelli EP 2004 Image quality assessment: from error visibility to structural similarity *IEEE transactions on image processing : a publication of the IEEE Signal Processing Society* 13 600–12 [PubMed: 15376593]
- Wu B, Ricchetti F, Sanguineti G, Kazhdan M, Simari P, Chuang M, Taylor R, Jacques R and McNutt T 2009 Patient geometry-driven information retrieval for IMRT treatment plan quality control *Med Phys* 36 5497–505 [PubMed: 20095262]
- Wu B, Ricchetti F, Sanguineti G, Kazhdan M, Simari P, Jacques R, Taylor R and McNutt T 2011 Data-driven approach to generating achievable dose-volume histogram objectives in intensity-modulated radiotherapy planning *Int J Radiat Oncol Biol Phys* 79 1241–7 [PubMed: 20800382]
- Yang D, Brame S, El Naqa I, Aditya A, Wu Y, Goddu SM, Mutic S, Deasy JO and Low DA 2011 Technical note: DIRART--A software suite for deformable image registration and adaptive radiotherapy research *Med Phys* 38 67–77 [PubMed: 21361176]

Figure 1.

Workflow of atlas construction and dose prediction in this study. Dashed part indicates the process of atlas construction. W_i : weighting factor for patient i ; DIR: Deformable image registration; DVF: Deformable vector field; Σ_i : summation of atlas patients.

Figure 2.

Comparison of cumulative DVHs between clinical and predicted plans for breast cancer patients (prescribed dose 50Gy) (a) number 7 and (b) number 14, prostate cancer patients (prescribed dose 70Gy) (c) number 4 and (d) number 5.

Figure 3.
Dose distribution comparison for breast patients number 7 (first row) and number 14 (second row) and prostate patients number 4 (third row) and number 5 (fourth row). Color bars are shown in Gy.

Figure 4. Comparison of DVH parameters (mean $\pm$ sd) between clinical and predicted plans for (a) breast cancer (n=18) and (b) prostate cancer (n=15) patients. CL-Breast: contralateral breast; Lt FH: left femoral head; Rt FH: right femoral head.

Figure 5. Absolute dose difference (mean $\pm$ sd) between clinical and predicted plans for (a) all breast patients and (b) all prostate patients. The x-axis represents patient number.

Figure 6: Cumulative DVH of predicted plans for a typical breast cancer patient using various atlas sizes (2, 5, 10 and 17 samples). (a) PTV, (b) heart, (c) lungs, (d) contralateral breast and (e) spinal cord.

Table 1.Impact of atlas size on dose prediction for 5 breast cancer patients (mean $\pm$ sd).

Parameters	2 samples	5 samples	10 samples	17 samples
PTV D _{95%} (Gy)	47.1 $\pm$ 0.3	47.4 $\pm$ 0.2	47.2 $\pm$ 0.5	46.6 $\pm$ 0.5
Heart V _{22.5} (%)	10.3 $\pm$ 2.9	6.3 $\pm$ 2.0	5.2 $\pm$ 1.7	5.3 $\pm$ 2.1
Lungs V ₂₀ (%)	12.3 $\pm$ 1.4	11.1 $\pm$ 1.5	11.4 $\pm$ 1.6	11.2 $\pm$ 1.6
Contralateral Breast V ₅ (%)	38.1 $\pm$ 5.2	34.6 $\pm$ 9.6	33.5 $\pm$ 9.1	28.4 $\pm$ 10.3
Spinal cord D _{max} (Gy)	8.7 $\pm$ 0.9	8.1 $\pm$ 0.7	9.5 $\pm$ 0.8	5.2 $\pm$ 0.5