2020

Characterization of Respiration-Induced Motion in Prone Versus Supine Patient Positioning for Thoracic Radiation Therapy

Christopher L. Guy
Virginia Commonwealth University, christopher.guy@vcuhealth.org

Elisabeth Weiss
Virginia Commonwealth University

Mihaela Rosu-Bubulac
Virginia Commonwealth University

Advances in Radiation Oncology (2020) 5, 466-472

advances in radiation oncology

www.advancesradonc.org

Scientific Article

Characterization of Respiration-Induced Motion in Prone Versus Supine Patient Positioning for Thoracic Radiation Therapy

Christopher L. Guy, PhD,* Elisabeth Weiss, MD, and Mihaela Rosu-Bubulac, PhD

Department of Radiation Oncology, Virginia Commonwealth University, Richmond, Virginia

Received 22 May 2019; revised 11 November 2019; accepted 14 February 2020

Abstract

Purpose: Variations in the breathing characteristics, both on short term (intrafraction) and long term (interfraction) time scales, may adversely affect the radiation therapy process at all stages when treating lung tumors. Prone position has been shown to improve consistency (ie, reduced intrafraction variability) and reproducibility (ie, reduced interfraction variability) of the respiratory pattern with respect to breathing amplitude and period as a result of natural abdominal compression, with no active involvement required from the patient. The next natural step in investigating breathing-induced changes is to evaluate motion amplitude changes between prone and supine targets or organs at risk, which is the purpose of the present study.

Methods and Materials: Patients with lung cancer received repeat helical 4-dimensional computed tomography scans, one prone and one supine, during the same radiation therapy simulation session. In the maximum-inhale and maximum-exhale phases, all thoracic structures were delineated by an expert radiation oncologist. Geometric centroid trajectories of delineated structures were compared between patient orientations. Motion amplitude was measured as the magnitude of difference in structure centroid position between inhale and exhale.

Results: Amplitude of organ motion was larger when the patient was in the prone position compared with supine for all structures except the lower left lobe and left lung as a whole. Across all 12 patients, significant differences in mean motion amplitude between orientations were identified for the right lung (3.0 mm, $P = .01$), T2 (0.5 mm, $P = .01$) and T12 (2.1 mm, $P < .001$) vertebrae, the middle third of the esophagus (4.0 mm, $P = .03$), and the lung tumor (1.7 mm, $P = .02$).

Conclusions: Respiration-induced thoracic organ motion was quantified in the prone position and compared with that of the supine position for 12 patients with thoracic lesions. The prone position induced larger organ motion compared with supine, particularly for the lung tumor, likely requiring increases in planning margins compared with supine.

Introduction

A recent study has revealed that a patient's breathing is more consistent, according to the stability of amplitude and period of their respiratory tract, when the patient is in prone position compared with supine[1] and is just one of many consequences of the difference in orientation.

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Sources of support: No funding was received for the conduct of this work.

Disclosures: Dr Weiss reports grants from the National Institutes of Health, grants from Varian, and royalties from UpToDate outside the submitted work. All other authors have nothing to disclose.

* Corresponding author: Christopher L. Guy, PhD; E-mail: christopher.guy@vcuhealth.org.

https://doi.org/10.1016/j.adro.2020.02.004

Placing a patient in the prone position for radiation therapy, as opposed to the standard supine position, induces anatomic changes that may also affect the patient's physiology. The heart and great vessels are displaced anteriorly, causing a much larger area of the heart to have contact with the chest wall and reducing respiration-induced heart movement.[2,3] The esophagus-to-spinal cord separation also increases compared with the supine position.[4,5] The prone position minimizes the volume of lung tissue between the heart and chest wall, which would otherwise be subject to greater pressure from the heart and abdomen.[6,7] In turn, the lungs become evenly aerated owing to a more homogeneous distribution of pleural pressures throughout the lungs.[6,8,9]

The utilization of the prone position in radiation therapy of the chest has been thoroughly investigated for the treatment of breast cancer. Particularly for large-breasted patients, the face-down orientation enables superior lung and chest wall dose sparing.[10-23] Cosmetic outcomes have also been reported to improve with the prone position compared with patients treated supine.[16,24,25] Some investigations have demonstrated reduced skin toxicity,[24,26] whereas others have reported opposite effects.[20,27] For pelvic radiation therapy, the use of the advantage of the prone position has been clearly demonstrated for reducing dose to uninvolved rectum and small bowel.[28,29] Although dosimetry may be improved for breast and pelvis treatments, the prone position results in larger setup errors, which must be accounted for in target margins.[10,30-32] The demonstrated benefit of prone for other treatment sites in the chest has not been as clear.

Spinal lesions can be treated more accurately and efficiently with lower organ-at-risk doses when the patient is in the prone position.[33,34] However, the supine position has been demonstrated to be more accurate, reproducible, and comfortable for the patients with better immobilization options.[35,36] Additionally, respiration-induced abdominal organ motion increases with the prone position[2] with the exception of kidneys, which are unaffected.[37]

Knowing that the prone patient orientation causes increased consistency in respiration,[1] the next step of investigation is to characterize the organ motion to determine whether the increased consistency of breathing may justify the use of prone position for treatment of lung tumors. The quantification of respiration-induced organ motion has thus far been primarily limited to the supine position for thoracic,[38-43] abdominal,[44-46] and pelvic[47] regions of interest. To the best of the author's knowledge, 4-dimensional motion of thoracic organs has not been reported for the prone patient orientation. The purpose of this study is to characterize thoracic organ motion (eg, for esophagus, lung and mediastinum tumors but excluding breast cancer) in the prone treatment position.

Material and Methods

Patient data

Patients undergoing radiation therapy for lung cancer for either palliative or curative treatment between 2010 and 2013 were eligible for enrollment on an institutional review board–approved imaging protocol in which helical 4-dimensional computed tomography scans were acquired using a Philips CT Big Bore simulator (Philips North America Corporation, Andover, MA) and the Varian Real-Time Position Management system (Varian Medical Systems, Inc, Palo Alto, CA) in both the prone and supine positions within the same imaging session. The system used an external marker block, placed on the patient's chest for supine and on the patient's back for prone, to generate a breathing trace for phase sorting. Although the motion amplitude of the block was reduced for supine compared with prone, a reliable breathing pattern was able to be extracted in both patient orientations without issue. Patients were positioned flat on the simulator couch for supine scans and with a 15-degree wedge cushion for chest support when prone. No other immobilization devices were used. Resulting images were free of major respiration-induced artifacts; therefore, the scans were of acceptable quality and appropriate for motion tracking of anatomy.

Twelve patients were selected sequentially for inclusion in this study. Tumor and normal tissue structures (right lung, left lung, esophagus, heart, T2, T5, and T12) were contoured by a physician on the end-of-inhale and end-of-exhale respiratory phases for all images using an in-house contouring protocol. Individual lung lobes were delineated, and the esophagus was also evenly divided into upper, middle, and lower sections based on the total number of axial slices traversed by the organ for intra-organ motion analysis. No contrast was used for esophagus visualization.

Motion analysis

Respiration-induced organ motion was analyzed by taking the position of the geometric centroid of each delineated organ structure and calculating the magnitude of displacement of the centroid between inhale and exhale breathing phases for each patient. Deformable image registration was performed between the 2 respiratory phases and orientations to qualitatively assess motion induced by respiration within the thorax by looking at the deformation vector field and spatial Jacobian images of the resulting transformation. A multilevel b-spline based parametric image registration was performed using the elastix registration software (http://elastix.isi.uu.nl/).[48,49] The supine inhale phase

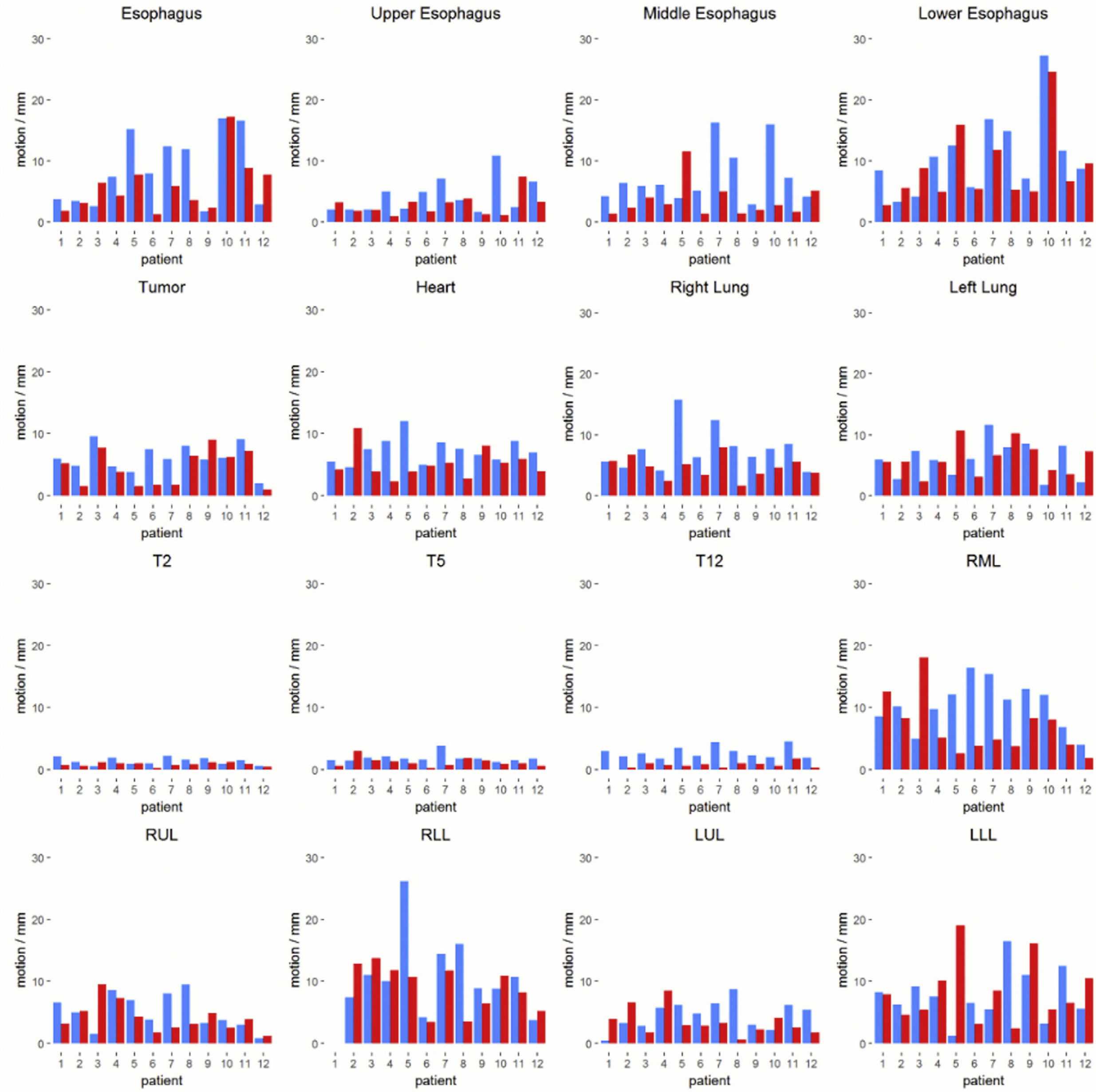

Figure 1 Motion amplitude of organ geometric centroids. Respiration-induced motion amplitude is shown for the prone (blue) and supine (red) orientations across all 12 patients of the study.

was separately registered to the supine exhale, prone inhale, and prone exhale phases. Details of the image registration are described elsewhere.[50]

Statistical analysis

Differences in motion amplitude between patient orientations and respiratory phases were tested for significance using a paired, 2-sided Student *t* test with a significance level of 0.05. All statistical testing was performed using the open-source statistical package R 3.4.4 for Windows (Microsoft Corporation, Redmond, WA).

Results

Respiration-induced organ motion was evaluated for 12 patients with lung cancer to study the effect of prone orientation compared with supine. When averaged across all patients, motion was larger in amplitude for all investigated thoracic structures except the left lower lobe, and consequently the left lung as a whole which showed no difference on average, when in the prone position compared with the supine orientation. Variance of the difference in motion amplitude between the 2 patient orientations was relatively large, demonstrating that some patients had less motion when prone for particular structures. However, the change in motion amplitude was also not consistent for all organs for a given patient (ie, some organs increased motion in supine position while, simultaneously, other structures decreased in motion amplitude). The differences in motion amplitude for all organs are shown on a per-patient basis in Figure 1.

Some patterns emerged when the data for the entire patient cohort were examined. Despite the motion amplitude being small compared with other delineated structures, thoracic vertebrae moved more on average in prone than supine. And across all patients, the motion of the T12 vertebra increased in prone compared with supine without exception. The middle third of the esophagus showed the largest difference in motion between patient orientations out of all segments of the organ. The mean motion amplitude for lung tumors was over 2 mm larger for prone than for supine, with some patients showing differences of up to 5.8 mm, suggesting that there is a trade-off between the consistency of breathing (obtained with prone) and minimizing treatment margins, at least when the patient is in free breathing without guidance.

Table 1 summarizes the geometric centroid motion amplitude for all thoracic structures of interest for the prone and supine positions individually and the difference in total motion amplitude between the 2 orientations. As the differences in motion amplitude were calculated as the total prone motion minus the total supine motion, positive values correspond to increased motion in the prone position. The differences in motion amplitude between positions were statistically significant for the right lung ($P = .01$), T2 ($P = .01$), T12 ($P < .001$), tumor ($P = .02$), and the middle third of the esophagus ($P = .03$), with the prone position showing increased motion compared with supine. For lungs and the esophagus, intrapatient motion range increased according to the subvolume's proximity to the diaphragm (ie, lower lobes and lower esophagus varied in position more than upper lobes and upper esophagus) for both supine and prone orientations.

Qualitative assessment of the deformations induced by change in patient orientation was performed after deformable image registration. Figure 2 illustrates the common characteristics observable when changing from prone to supine. The green deformation vectors indicate the tissue movement when changing from prone to supine. Anterior heart migration occurs in the prone position as evident by the increased contact of the heart and chest wall and the decrease of lung parenchyma separating the 2 structures. Decreased tissue compression in the posterior lung owing to the weight of the heart is observed as well when moving from supine to prone. Finally, increased diaphragm excursion was noticeable for all patients when in the prone position, as illustrated by the further-inferior diaphragm position compared with its location while supine.

Discussion

Most studies that have investigated organ motion in the thorax have been constrained to supine patient setups.[38,40-43] The supine organ motion reported in these investigations has been larger in magnitude than the excursions reported here. Hashimoto et al found esophagus displacements between 7.9 mm and 12.9 mm, with the

Table 1 Inhale-to-exhale motion amplitude of organ center of mass

Structure	Supine motion amplitude (mm)				Prone motion amplitude (mm)				Prone and supine difference (mm)				*P* value*
	Mean	Stdev	Min	Max	Mean	Stdev	Min	Max	Mean	Stdev	Min	Max	
RUL	4.1	2.4	1.2	9.5	5.1	2.8	0.8	9.5	1.0	3.7	−8.0	6.4	.40
RML	6.8	4.7	1.8	18.1	10.4	3.8	4.0	16.4	3.6	6.9	−13.1	12.6	.10
RLL	8.2	4.4	0.0	13.7	10.1	6.8	0.0	26.2	1.9	6.2	−5.5	15.5	.31
LUL	3.4	2.2	0.6	8.5	4.6	2.3	0.4	8.7	1.2	3.5	−3.6	8.1	.28
LLL	8.3	5.0	2.4	19.0	7.8	4.2	1.2	16.5	−0.5	7.7	−17.8	14.1	.82
R lung	4.6	1.8	1.6	7.9	7.6	3.5	3.9	15.7	3.0	3.3	−2.1	10.6	.01
L lung	6.0	2.6	2.3	10.7	5.9	3.0	1.8	11.6	0.0	4.0	−7.3	5.0	.97
T2	0.8	0.3	0.2	1.2	1.4	0.6	0.5	2.2	0.5	0.6	−0.6	1.5	.01
T5	1.2	0.7	0.2	3.0	1.8	0.7	1.2	3.8	0.7	1.1	−1.6	3.1	.06
T12	0.7	0.4	0.0	1.7	2.8	0.9	1.7	4.5	2.1	0.9	1.0	4.1	<.001
Heart	5.1	2.4	2.3	10.9	7.3	2.1	4.6	12.0	2.2	3.8	−6.3	8.1	.07
Lung tumor	4.4	2.9	1.0	9.0	6.1	2.2	2.0	9.6	1.7	2.2	−3.2	5.8	.02
Esophagus	5.8	4.4	1.2	17.2	8.6	5.8	1.7	17.0	2.7	4.6	−4.8	8.3	.07
Esophagus, upper	2.7	1.8	0.9	7.4	4.2	2.8	1.6	10.8	1.5	3.7	−5.0	9.7	.20
Esophagus, middle	3.4	2.9	1.3	11.5	7.4	4.5	2.9	16.3	4.0	5.6	−7.6	13.3	.03
Esophagus, lower	8.8	6.2	2.7	24.6	10.9	6.6	3.3	27.3	2.1	4.3	−4.7	9.6	.12

Abbreviations: LLL, left lower lobe; LUL, left upper lobe; RML, right middle lobe; RLL, right lower lobe; RUL, right upper lobe; Stdev = standard deviation.

* Paired, 2-sided Student *t* test at .05 significance level used to test difference in mean amplitudes.

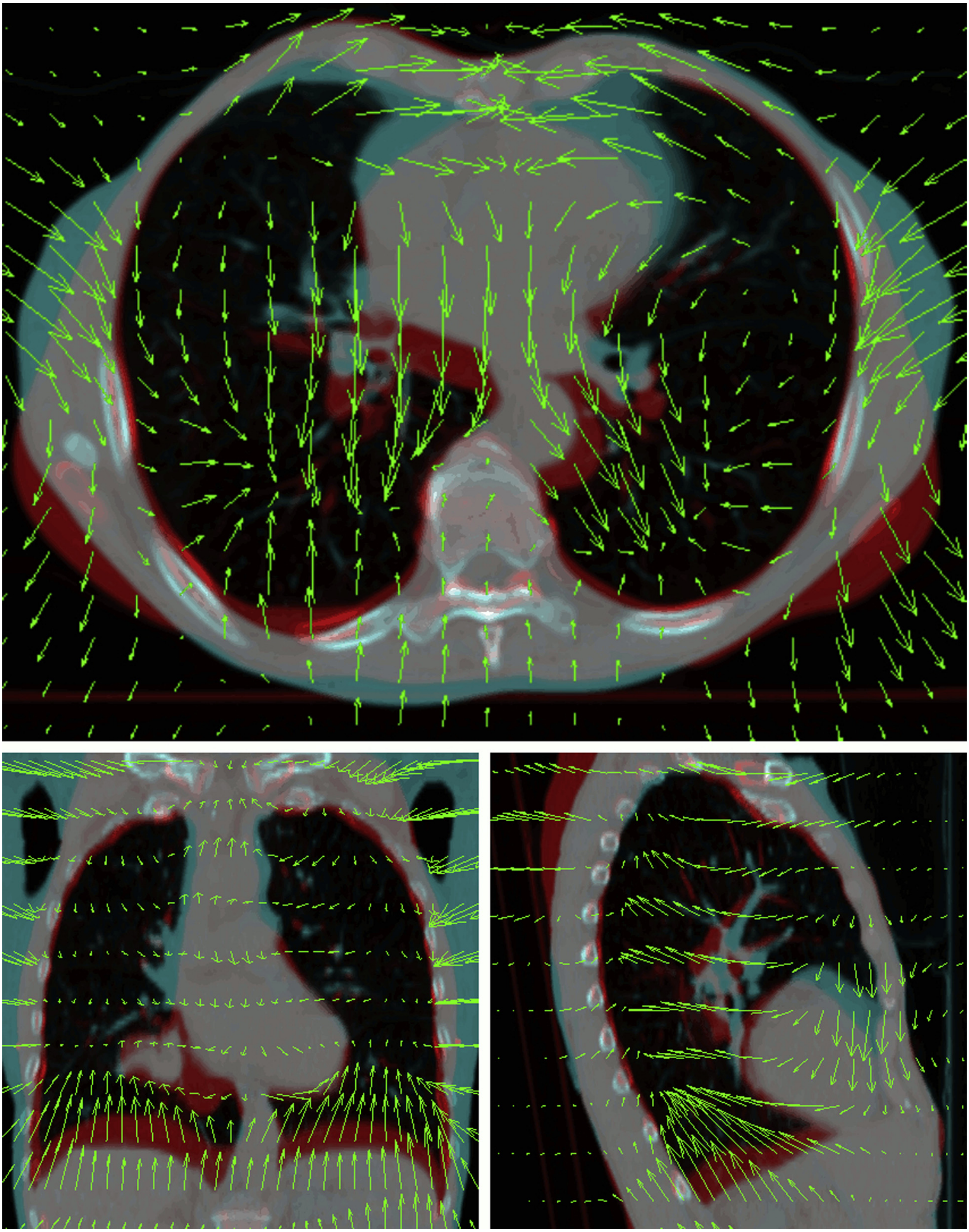

Figure 2 Deformation from change of patient orientation. Color overlay of the prone (blue) and supine (red) inhale phases for one patient of the study. Deformation shown in the figure is the result of changing from prone to supine patient orientation and vice versa. The deformation vector field (arrows) obtained from deformable image registration is shown illustrating the effects of the change in orientation. The increased dorsal compression posterior to the mediastinum while supine is observed in the axial image, and anterior heart migration was also evident. Reduced diaphragm excursion while supine can be seen in the sagittal and coronal views.

lower esophagus showing the greatest motion compared with the 2.7- to 8.8-mm range of total motion found in our supine patient data set.[45] Perhaps the most in-depth investigation of thoracic organ motion was performed by Weiss et al using 4-dimensional computed tomography acquisitions of patients with lung cancer, as done in the present work.[47] The motion reported in their study was comparable to the supine results reported here but limited to the supine orientation.

Unlike the breast for which motion is reduced when the patient is prone,[51] most thoracic structures show significantly greater respiration-induced motion in prone position. For esophagus primaries, Dieleman et al determined necessary margins of 5 mm, 6 to 7 mm, and 8 to 9 mm for upper, middle, and lower esophageal lesions, respectively.[42] The mean displacements of the middle and lower esophagus of 7.9 mm and 10.2 mm, respectively, exceeded these margins when the patient was prone in the current data set, although choosing a midrespiratory phase for treatment planning would likely bring prone motion within these margins.

This investigation was prompted by the findings that breathing patterns of patients are more consistent when the patient is prone than supine, with consistency defined by the repeatability of breathing cycle amplitude and period in addition to several other metrics.[1] By analyzing the organ motion, this study sought to induce the effect of prone position on motion amplitude for all structures of the thorax (excluding breast) and to determine whether the findings justify further investigation of prone position for use in radiation therapy treatments of the thorax. Based on the results reported here, the increased organ motion observed on average across all patients was not complementary to the improved patient breathing and would not justify the use of prone to treat tumors in this region of the body, although additional dosimetric investigation would be necessary to definitively assess this suspicion. Despite the lack of promise prone orientation shows for more conformal radiation therapy treatments due to increased motion, this study was able to quantify respiratory motion of thoracic structures when prone and perform direct comparison to the supine orientation for context.

Conclusions

Respiratory-induced organ motion is of greater magnitude in the prone position compared with supine. Owing to the increased tumor motion in the prone position, the supine orientation is likely more advantageous for lung targets in minimizing treatment margins, despite improved breathing consistency in the prone position. A future treatment planning study would be necessary to quantify the dosimetric differences between prone and supine plans for specific treatment sites within thorax.

References

1. Ostyn M, Weiss E, Rosu-Bubulac M. Respiratory cycle characterization and optimization of amplitude-based gating parameters for prone and supine lung cancer patients. *Biomed Phys Eng Express*. 2020;6:3.
2. Ball W, Wicks J, Mettler F. Prone-supine change in organ position: CT demonstration. *Am J Roentgenol*. 1980;135:815-820.
3. Lakosi F, Gulyban A, Janvary L, et al. Respiratory motion, anterior heart displacement and heart dosimetry: Comparison between prone (Pr) and supine (Su) whole breast irradiation. *Pathol Oncol Res*. 2015;21:1051-1058.
4. Corn BW, Coia LR, Chu JC, et al. Significance of prone positioning in planning treatment for esophageal cancer. *Int J Radiat Oncol Biol Phys*. 1991;21:1303-1309.
5. Vijayakumar S, Muller-Runkel R. Irradiation of the thoracic esophagus prone versus supine treatment positions. *Acta Radiol Oncol*. 1986;25:187-189.
6. Albert RK, Hubmayr RD. The prone position eliminates compression of the lungs by the heart. *Am J Respir Crit Care Med*. 2000; 161:1660-1665.
7. Chino JP, Marks LB. Prone positioning causes the heart to be displaced anteriorly within the thorax: implications for breast cancer treatment. *Int J Radiat Oncol Biol Phys*. 2008;70:916-920.
8. Kallet RH. A comprehensive review of prone position in ARDS. *Respir Care*. 2015;60:1660-1687.
9. Pelosi P1, Tubiolo D, Mascheroni D, et al. Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury. *Am J Respir Crit Care Med*. 1998;157:387-393.
10. Kirby AM1, Evans PM, Donovan EM, et al. Prone versus supine positioning for whole and partial-breast radiotherapy: A comparison of non-target tissue dosimetry. *Radiother Oncol*. 2010;96: 178-184.
11. Formenti SC, DeWyngaert JK, Jozsef G, Goldberg JD. Prone vs supine positioning for breast cancer radiotherapy. *JAMA*. 2012;308: 861-863.
12. Lymberis SC, deWyngaert JK, Parhar P, et al. Prospective assessment of optimal individual position (prone versus supine) for breast radiotherapy: Volumetric and dosimetric correlations in 100 patients. *Int J Radiat Oncol Biol Phys*. 2012;84:902-909.
13. Ramella S, Trodella L, Ippolito E, et al. Whole-breast irradiation: A subgroup analysis of criteria to stratify for prone position treatment. *Med Dosim*. 2012;37:186-191.
14. Fernández-Lizarbe E, Montero A, Polo A, et al. Pilot study of feasibility and dosimetric comparison of prone versus supine breast radiotherapy. *Clin Transl Oncol*. 2013;15:450-459.
15. Krengli M, Masini L, Caltavuturo T, et al. Prone versus supine position for adjuvant breast radiotherapy: A prospective study in patients with pendulous breasts. *Radiat Oncol*. 2013;8:232.
16. Osa EO, DeWyngaert K, Roses D, et al. Prone breast intensity modulated radiation therapy: 5-year results. *Int J Radiat Oncol Biol Phys*. 2014;89:899-906.
17. Verhoeven K, Sweldens C, Petillion S, et al. Breathing adapted radiation therapy in comparison with prone position to reduce the doses to the heart, left anterior descending coronary artery, and contralateral breast in whole breast radiation therapy. *Pract Radiat Oncol*. 2014;4:123-129.
18. Guenzi M, Bosetti D, Lamanna G, et al. Novel 10-fraction breast irradiation in prone and supine position: Technical, dosimetric and clinical evaluation. *Tumori*. 2015;101:154-160.
19. Shin SM, No HS, Vega RM, et al. Breast, chest wall, and nodal irradiation with prone set-up: Results of a hypofractionated trial with a median follow-up of 35 months. *Pract Radiat Oncol*. 2016;6:e81-e88.
20. Takahashi K, Morota M, Kagami Y, et al. Prospective study of postoperative whole breast radiotherapy for Japanese large-breasted

women: A clinical and dosimetric comparisons between supine and prone positions and a dose measurement using a breast phantom. *BMC Cancer*. 2016;16:757.
21. Deseyne P, Speleers B, De Neve W, et al. Whole breast and regional nodal irradiation in prone versus supine position in left sided breast cancer. *Radiat Oncol*. 2017;12:89.
22. Dundas K, Pogson EM, Batumalai V, et al. The impact of imaging modality (CT vs MRI) and patient position (supine vs prone) on tangential whole breast radiation therapy planning. *Pract Radiat Oncol*. 2018;8:e87-e97.
23. Charaghvandi KR, Van't Westeinde T, Yoo S, et al. Single dose partial breast irradiation using an MRI linear accelerator in the supine and prone treatment position. *Clin Transl Radiat Oncol*. 2018; 14:1-7.
24. McKinnon R, Christie D, Peres H, Burke M, Le T, Lah M. The prone technique for breast irradiation: Is it ready for clinical trials? *Breast*. 2009;18:30-34.
25. Veldeman L, Schiettecatte K, De Sutter C, et al. The 2-year cosmetic outcome of a randomized trial comparing prone and supine whole-breast irradiation in large-breasted women. *Int J Radiat Oncol Biol Phys*. 2016;95:1210-1217.
26. Mulliez T, Veldeman L, van Greveling A, et al. Hypofractionated whole breast irradiation for patients with large breasts: A randomized trial comparing prone and supine positions. *Radiother Oncol*. 2013;108:203-208.
27. Varga Z, Hideghéty K, Mezo T, Nikolényi A, Thurzó L, Kahán Z. Individual positioning: A comparative study of adjuvant breast radiotherapy in the prone versus supine position. *Int J Radiat Oncol Biol Phys*. 2009;75:94-100.
28. Zelefsky MJ, Happersett L, Leibel SA, et al. The effect of treatment positioning on normal tissue dose in patients with prostate cancer treated with three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys*. 1997;37:13-19.
29. I Das IJ, Lanciano RM, Movsas B, Kagawa K, Barnes SJ. Efficacy of a belly board device with CT-simulation in reducing small bowel volume within pelvic irradiation fields. *Int J Radiat Oncol Biol Phys*. 1997;39:67-76.
30. Stroom JC, Koper PC, Korevaar GA, et al. Internal organ motion in prostate cancer patients treated in prone and supine treatment position. *Radiother Oncol*. 1999;51:237-348.
31. Weber DC, Nouet P, Rouzaud M, Miralbell R. Patient positioning in prostate radiotherapy: Is prone better than supine? *Int J Radiat Oncol Biol Phys*. 2000;47:365-371.
32. Bartlett FR, Colgan RM, Donovan EM, et al. The UK HeartSpare Study (Stage IB): Randomised comparison of a voluntary breath-hold technique and prone radiotherapy after breast conserving surgery. *Radiother Oncol*. 2015;114:66-72.
33. Descovich M, Ma L, Chuang CF, Larson DA, Barani IJ. Comparison between prone and supine patient setup for spine stereotactic body radiosurgery. *Technol Cancer Res Treat*. 2012;11:229-236.
34. Fürweger C, Drexler C, Muacevic A, Wowra B, de Klerck EC, Hoogeman MS. CyberKnife robotic spinal radiosurgery in prone position: Dosimetric advantage due to posterior radiation access? *J Appl Clin Med Phys*. 2014;15:4427.
35. Hideghéty K, Cserháti A, Nagy Z, et al. A prospective study of supine versus prone positioning and whole-body thermoplastic mask fixation for craniospinal radiotherapy in adult patients. *Radiother Oncol*. 2012;102:214-218.
36. Verma J, Mazloom A, Teh BS, South M, Butler EB, Paulino AC. Comparison of supine and prone craniospinal irradiation in children with medulloblastoma. *Pract Radiat Oncol*. 2015;5:93-98.
37. Pham D, Kron T, Foroudi F, Schneider M, Siva S. A review of kidney motion under free, deep and forced-shallow breathing conditions: Implications for stereotactic ablative body radiotherapy treatment. *Technol Cancer Res Treat*. 2014;13:315-323.
38. Wang Y, Riederer SJ, Ehman RL. Respiratory motion of the heart: Kinematics and the implications for the spatial resolution in coronary imaging. *Magn Reson Med*. 1995;33:713-719.
39. Shechter G, Ozturk C, Resar JR, McVeigh ER. Respiratory motion of the heart from free breathing coronary angiograms. *IEEE Trans Med Imaging*. 2004;23:1046-1056.
40. Gagel B, Demirel C, Kientopf A, et al. Active breathing control (ABC): Determination and reduction of breathing-induced organ motion in the chest. *Int J Radiat Oncol Biol Phys*. 2007;67:742-749.
41. Giraud P, De Rycke Y, Dubray B, et al. Conformal radiotherapy (CRT) planning for lung cancer: Analysis of intrathoracic organ motion during extreme phases of breathing. *Int J Radiat Oncol Biol Phys*. 2001;51:1081-1092.
42. Dieleman EM, Senan S, Vincent A, et al. Four-dimensional computed tomographic analysis of esophageal mobility during normal respiration. *Int J Radiat Oncol Biol Phys*. 2007;67:775-780.
43. Weiss E, Wijesooriya K, Dill SV, Keall PJ. Tumor and normal tissue motion in the thorax during respiration: Analysis of volumetric and positional variations using 4D CT. *Int J Radiat Oncol Biol Phys*. 2007;67:296-307.
44. Yang GY, McClosky SA, Khushalani NI. Principles of modern radiation techniques for esophageal and gastroesophageal junction cancers. *Gastrointest Cancer Res*. 2009;3(2 Suppl):S6-S10.
45. Hashimoto T, Shirato H, Kato M, Yamazaki K, et al. Real-time monitoring of a digestive tract marker to reduce adverse effects of moving organs at risk (OAR) in radiotherapy for thoracic and abdominal tumors. *Int J Radiat Oncol Biol Phys*. 2005;61:1559-1564.
46. Kim YS, Park SH, Ahn SD, et al. Differences in abdominal organ movement between supine and prone positions measured using four-dimensional computed tomography. *Radiother Oncol*. 2007;85:424-428.
47. Weiss E, Vorwerk H, Richter S, Hess CF. Interfractional and intrafractional accuracy during radiotherapy of gynecologic carcinomas: A comprehensive evaluation using the ExacTrac system. *Int J Radiat Oncol Biol Phys*. 2003;56:69-79.
48. Klein S, Staring M, Murphy K, Viergever MA, Pluim JP. Elastix: A Toolbox for intensity-based medical image registration. *IEEE Trans Med Imaging*. 2010;29:196-205.
49. Shamonin DP, Bron EE, Lelieveldt BP, et al. Fast parallel image registration on CPU and GPU for diagnostic classification of Alzheimer's disease. *Front Neuroinform*. 2014;7:50.
50. Guy CL, Weiss E, Che S, Jan N, Zhao S, Rosu-Bubulac M. Evaluation of image registration accuracy for tumor and organs at risk in the thorax for compliance with TG 132 recommendation. *Adv Radiat Oncol*. 2019;4:177-185.
51. Veldeman L, De Gersem W, Speleers B, et al. Alternated prone and supine whole-breast irradiation using IMRT: Setup precision, respiratory movement and treatment time. *Int J Radiat Oncol Biol Phys*. 2012;82:2055-2064.