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Scientific Article

Application of Continuous Positive Airway Pressure for Thoracic Respiratory Motion Management: An Assessment in a Magnetic Resonance Imaging−Guided Radiation Therapy Environment

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Abstract

Purpose: Patient tolerability of magnetic resonance (MR)−guided radiation treatment delivery is limited by the need for repeated deep inspiratory breath holds (DIBHs). This volunteer study assessed the feasibility of continuous positive airway pressure (CPAP) with and without DIBH for respiratory motion management during radiation treatment with an MR-linear accelerator (MR-linac).

Methods and Materials: MR imaging safety was first addressed by placing the CPAP device in an MR-safe closet and configuring a tube circuit via waveguide to the magnet bore. Reproducibility and linearity of the final configuration were assessed. Six healthy volunteers underwent thoracic imaging in a 0.35T MR-linac, with one free breathing (FB) and 2 DIBH acquisitions being obtained at 5 pressures from 0 to 15 cm-H_2O. Lung and heart volumes and positions were recorded; repeatability was assessed by comparing 2 consecutive DIBH scans. Blinded reviewers graded images for motion artifact using a 3-point grading scale. Participants completed comfort and perception surveys before and after imaging sessions.

Results: Compared with FB alone, FB-10, FB-12, and FB-15 cm H_2O significantly increased lung volumes (+23%, +34%, +44%; all $P <.05$) and inferiorly displaced the heart (0.86 cm, 0.96 cm, 1.18 cm; all $P < .05$). Lung volumes were significantly greater with DIBH-0 cm H_2O compared with FB-15 cm H_2O (+105% vs +44%, $P = .01$), and DIBH-15 cm H_2O yielded additional volume increase (+131% vs +105%, $P = .01$). Adding CPAP to DIBH decreased lung volume differences between consecutive breath holds (correlation coefficient 0.97 at 15 cm H_2O vs 0.00 at 0 cm H_2O). The addition of 15 cm H_2O CPAP reduced artifact scores ($P = .03$) compared with FB; all DIBH images (0-15 cm H_2O) had less artifact ($P < .01$).

Conclusions: This work demonstrates the feasibility of integrating CPAP in an MR-linac environment in healthy volunteers. Extending this work to a larger patient cohort is warranted to further establish the role of CPAP as an alternative and concurrent approach to DIBH in MR-guided radiation therapy.

Introduction

Deep inspiratory breath hold (DIBH) has been a clinically validated approach for the management of respiratory motion during the delivery of radiation therapy. During DIBH, lung volume increases, resulting in 2 major benefits: (1) targets typically affected by respiration (ie, lung, breast, liver, or abdominal lesions) have reduced excursion, thereby reducing the overall target volume requiring radiation; and (2) sensitive organs at risk such as the heart move away from the radiation treatment fields, thus reducing the dose.[1,2] Although dosimetrically favorable, DIBH requires a high degree of patient cooperation to successfully deliver. Furthermore, it is time consuming and its use increases treatment delivery times.[3]

Many clinics use additional techniques such as active breathing control or spirometers to improve repeatability of breath holds.[4] However, this strategy depends on patient compliance, involves longer treatment times, and uses more clinical resources.[4,5] Although motion can be limited through modulation of respiration, it can also be accounted for through use of medical imaging in the treatment room for real-time localization of the tumor.[6] ViewRay Inc (Cleveland, OH) designed a Co-60 based integrated magnetic resonance (MR) 0.35 T–guided radiation delivery system in 2012 and subsequently was able to substitute the radioactive cobalt-based system with a 6MV linear accelerator (linac) –based integrated MR-guided system in 2017.[7] The Unity system (Elekta A.B., Stockholm, Sweden; Philips N.V., Amsterdam, Netherlands) is another linac in clinical use with on-board 1.5 T imaging capability.[8] The ability to obtain MR images during radiation treatments with these integrated systems allows better soft-tissue visualization and online adaptive treatment planning, and some systems allow real-time imaging-based treatment gating. Lesions can be tracked in real time (currently up to 8 frames/s) and respiratory gating can be performed based on internal anatomy. This technology has shown promise in facilitating delivery of dose-escalated stereotactic radiation treatments, where enhanced visualization of tumors and surrounding organs at risk allows for greater certainty of structure boundaries. Onboard magnetic resonance imaging (MRI) also provides near real-time verification of breath hold reliability,[9] which has been used clinically in treatments of tumors of the abdomen and thorax.[9-16] Nevertheless, challenges that remain include the need for repeated breath holds during the course

of these treatment sessions to deliver the daily dose and improving overall patient compliance. One intervention shown to improve reproducibility is incorporating audiovisual biofeedback[17] or real-time coaching.

Continuous positive airway pressure (CPAP) has been used widely and safely in patients in an ambulatory and home-care setting, most notably in the management of obstructive sleep apnea.[18] The CPAP device filters room air and uses a compressor to generate a set pressure of air which is subsequently delivered via nasal pillow, full face mask, or hybrid mask. This constant level of pressure throughout the respiratory cycle splints open the upper airway and prevents dynamic collapse. This mechanism has also been used sparingly in the radiation oncology setting as it is associated with increased end-expiratory volumes and decreased respiratory rate; however, it may also introduce larger tidal volumes and greater diaphragmatic movement.[19] A number of published early clinical experiences have reported deploying CPAP as a cost-effective and readily available respiratory management strategy during radiation therapy.[20-27] Here, the present work investigates the compatibility of the CPAP system with an MR-linac system while using the onboard MRI to characterize geometric changes and image quality under different CPAP-aided and DIBH conditions. Of significant interest was the effect of using CPAP as an adjunct to DIBH goal of investigating the interaction between breath holds and external airway pressure.

Methods and Materials

The ResMed S9 CPAP (ResMed Inc, San Diego, CA) was used to provide airway pressures. The heated humidifier attachment was not used in this study. The CPAP was placed in a radiofrequency shielded closet near the ViewRay MR-linac and a 5-circuit (7.3 m) configuration of single-use extension tubing was fitted through a shielded waveguide to yield the necessary length to reach the center of the MRI bore. CPAP linearity (response between inputted cm H_2O setting and measured with a manometer) of the 5-circuit configuration was obtained before each volunteer imaging session. Reproducibility (repeated measures at 0, 15, and 20 cm-H_2O) data were obtained to characterize the device reliability. A baseline correction of + 2 cm-H_2O was necessary for all pressure settings.
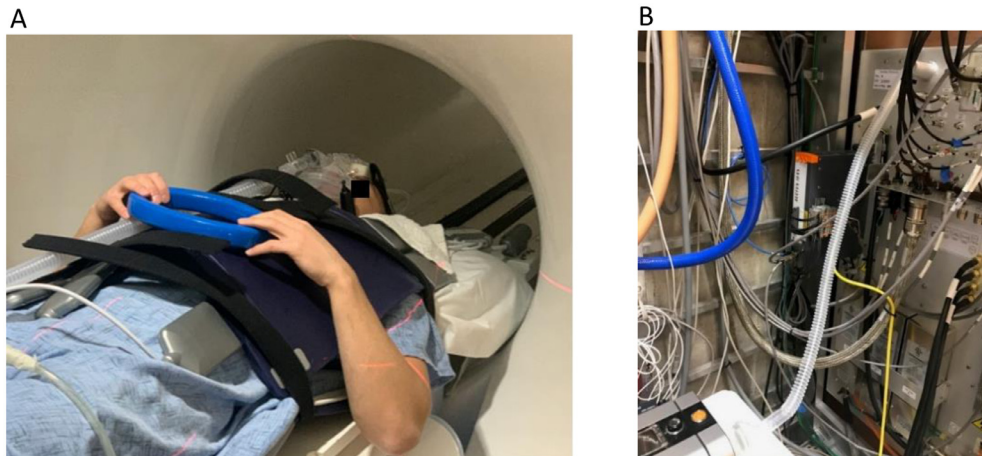
Figure 1 Healthy volunteer setup for continuous positive airway pressure (CPAP) evaluation in a magnetic resonance −guided radiation therapy environment **(A)** including the torso coils, immobilization devices, CPAP mask, and **(B)** circuit tubing that was run through a waveguide to a radiofrequency shielded closet between the CPAP machine and magnetic resonance imaging room.

With each volunteer study, a new 5-circuit tubing configuration was built and before imaging studies, actual delivered airway pressures were recorded at each planned level of pressure: 0, 6, 10, 12, and 15 cm H_2O to ensure build reliability. Healthy volunteers at our institution were enrolled from October 2019 through February 2020 to participate in an institutional review board−approved pilot study. The study was halted in March 2020 because of the COVID-19 pandemic, and further recruitment was not possible given the respiratory nature of the study. Participants were adults (age >18) who provided study-specific informed consent; individuals were excluded if they had history of recent esophageal surgery, chronic obstructive pulmonary disease, heart failure, recent facial trauma or facial surgery, psychiatric limitations preventing MRI or CPAP mask, current pregnancy, MRI-incompatible implants, or inability to provide consent. Registration was done only after eligibility assessment was complete and criteria were met, including MRI safety screening. A total of 6 adult males met the inclusion criteria and participated in the study.

Volunteers were then fitted by a physician or respiratory therapist with an oronasal facemask (Phillips Respironics Inc, Murrysville, PA). Initial comfort and tolerability testing was conducted by applying CPAP at pressures of 0 cm H_2O up to 15 cm H_2O. After 2 minutes at each pressure, volunteers were asked if the current pressure was tolerable and if they would be willing to raise the pressure to the next setting. All volunteers then completed a 6-question subjective survey graded on a 10-point scale (1 strongly disagree to 10 strongly agree), with 3 questions pertaining to patient comfort and the other 3 questions to patient attitudes and perceptions of their CPAP experience.

After the initial CPAP tolerability evaluation, thoracic images were obtained using the MRIdian ViewRay MR-guided linac (double-donut superconducting 70 cm wide bore, 0.35 T 50 cm FOV magnet). Torso MRI coils, CPAP mask, and ear protection were placed and secured. Participants were imaged lying supine, head-first into the bore, with arms holding a foam ring at the abdomen and with a knee sponge for comfort as shown in Figure 1. Volumetric MRIs were obtained at each pressure level with a 25-second free breathing (FB) scan followed by 2 repeated 25-second DIBH scans (25 second TrueFISP, $1.5 \times 1.5 \times 3$ mm^3 resolution). Breath holds were coached by verbal instruction without audio-visual feedback. After the imaging session, the participants completed the same survey that was administered after the initial CPAP tolerability evaluation. The heart, left lung, and right lung were contoured by a radiation oncologist on the MR images in MIM version 6.8.7 (MIM Software Inc, Cleveland, OH) and subsequently reviewed by a medical physicist. Volumes and positional centroids of heart and lungs were automatically extracted using an in-house script. Organ displacement was determined by rigid registration (translations only) based on bony anatomy to establish a mutual coordinate system between successive data sets to the reference condition (FB-0 cm H_2O).

The presence of motion artifacts was assessed by a consensus of 2 scorers (a radiation oncologist and a medical physicist) for each data set acquired. The scorers were blinded as to which image was being shown and the motion-associated liver dome artifact was graded on a scale from 0 to 2. A score of 0 was assigned to images with no appreciable motion artifact blurring, a score of 1 to images with mild-moderate motion artifact blurring, and a score of 2 to images with major motion artifact thereby limiting clinical use. For breath hold conditions at which 2 images were obtained, the average motion artifact score was calculated.

Table 1   Scores from participant questionnaires before and after imaging (N = 6)

	Preimaging mean (SD, range)	Postimaging mean (SD, range)	P value
Comfort questions (10 = most uncomfortable, 1 = least uncomfortable)			
How much difficulty did you have tolerating CPAP?	2.8 (1.3, 1-5)	2.0 (1.1, 1-4)	.04*
How uncomfortable was the mask?	2.2 (1.6, 1-5)	2.2 (1.2, 1-4)	1
How uncomfortable was the pressure?	3.5 (1.2, 3-6)	2.2 (1.9, 1-6)	.01*
Attitude questions (10 = most favorable, 1 = least favorable):			
What is the likelihood of you wearing the equipment for radiation treatment?	7.7 (1.6, 5-10)	9.0 (1.3, 8-10)	.16
How beneficial do you think the CPAP is going to be for side effects from the radiation?	7.2 (2.6, 4-10)	8.0 (1.7, 6-10)	.09
What is your attitude toward CPAP therapy?	8.2 (1.9, 5-10)	9.0 (1.3, 7-10)	.18

Abbreviations: CPAP = continuous positive airway pressure; SD = standard deviation.
*   Indicates $P < .05$.
Student 2-tailed paired *t* tests were used to generate *P* values.

Paired *t* tests were performed to compare the mean difference of lung and heart volumes to the baseline volumes at the reference condition. A similar analysis was performed on heart centroid displacement. Reference volumes and centroid locations for comparison were defined at the FB-0 cm H_2O condition, similar to the standard established in other CPAP studies.[20,23,24,27] Additional comparisons were done for FB-15 cm H_2O versus DIBH-0 cm H_2O as well as DIBH-0 cm H_2O versus DIBH-15 cm H_2O to assess the relative magnitude of geometric changes associated with CPAP alone, DIBH alone, and the combination of the 2. Paired *t* tests were also used to compare the subjective artifact grades of images at all conditions to the artifact grades of the reference condition image. A statistically significant difference was detected if the *P* value was less than .05 with 2-tailed paired *t* tests. The effect of CPAP on repeatability of breath hold was analyzed by comparing total lung volumes and superior/inferior heart centroid location of 2 consecutive breath holds at each pressure. Intraclass correlation coefficients (ICC) and their 95% confidence intervals (CI) were calculated to measure the variation in total lung volumes and inferior heart displacement as surrogates for repeatable breath holds. An ICC of 0 indicates no repeatability and an ICC of 1 indicates total repeatability; ICC values above 0.9 suggest excellent repeatability.

Results

A total of 6 healthy adult participants were enrolled in this pilot study from October 2019 through February 2020. All participants were males with a median age of 38 years (range, 28-54 years) and mean weight of 92 kg (range, 75-127 kg). All participants were able to tolerate CPAP up to the maximum pressure of 15 cm H_2O in both the CPAP tolerability evaluation and imaging sessions. Participant survey results from the prescan (during fit testing) and postscan questionnaires are summarized in Table 1. For questions that queried comfort, participants noted that they had less perceived difficulty tolerating CPAP after the imaging session compared with before the scan ($P = .04$). There was no change in mask comfort between the 2 surveys, but subjects were more acclimated to the pressure at the latter time point, with higher perceived comfort after the scan ($P = .01$). Attitude and perception questions are also shown in Table 1; none of these showed significantly different changes.

Of the 6 volunteers, 2 did not have images obtained at 6 cm H_2O pressure to reduce overall image study time but had images for all other pressures included in the final analysis. Anatomic changes seen with selected CPAP, breath hold, and combined conditions are shown with image overlays in Figure 2. Table 2 summarizes the geometric changes associated with these conditions. At FB-6, 10, 12, and 15 cm H_2O pressure, a mean total lung volume increase relative to the baseline reference condition (FB-0 cm H_2O) was observed of 14% ($P = .16$), 29% ($P = .02$), 34% ($P = .01$), and 44% ($P < .01$), respectively. An even greater increase in lung volume was seen with DIBH-0 cm H_2O, with a mean volume increase over baseline of 105%. Not only was this significant compared with baseline ($P < .01$), but it was also greater than the volume increase seen with FB-15 cm H_2O ($P = .01$). A 130% increase in lung volume over baseline was seen with CPAP-aided breath hold (DIBH-15 cm H_2O), greater than with breath hold alone (DIBH-0 cm H_2O; $P < .01$). Decreases in heart volume with CPAP alone and with breath hold alone did not reach statistical significance, but the decrease did reach significance with CPAP levels of ≥10 cm H_2O applied together with a breath hold. With CPAP-aided DIBH at 10, 12, and 15 cm H_2O, the mean
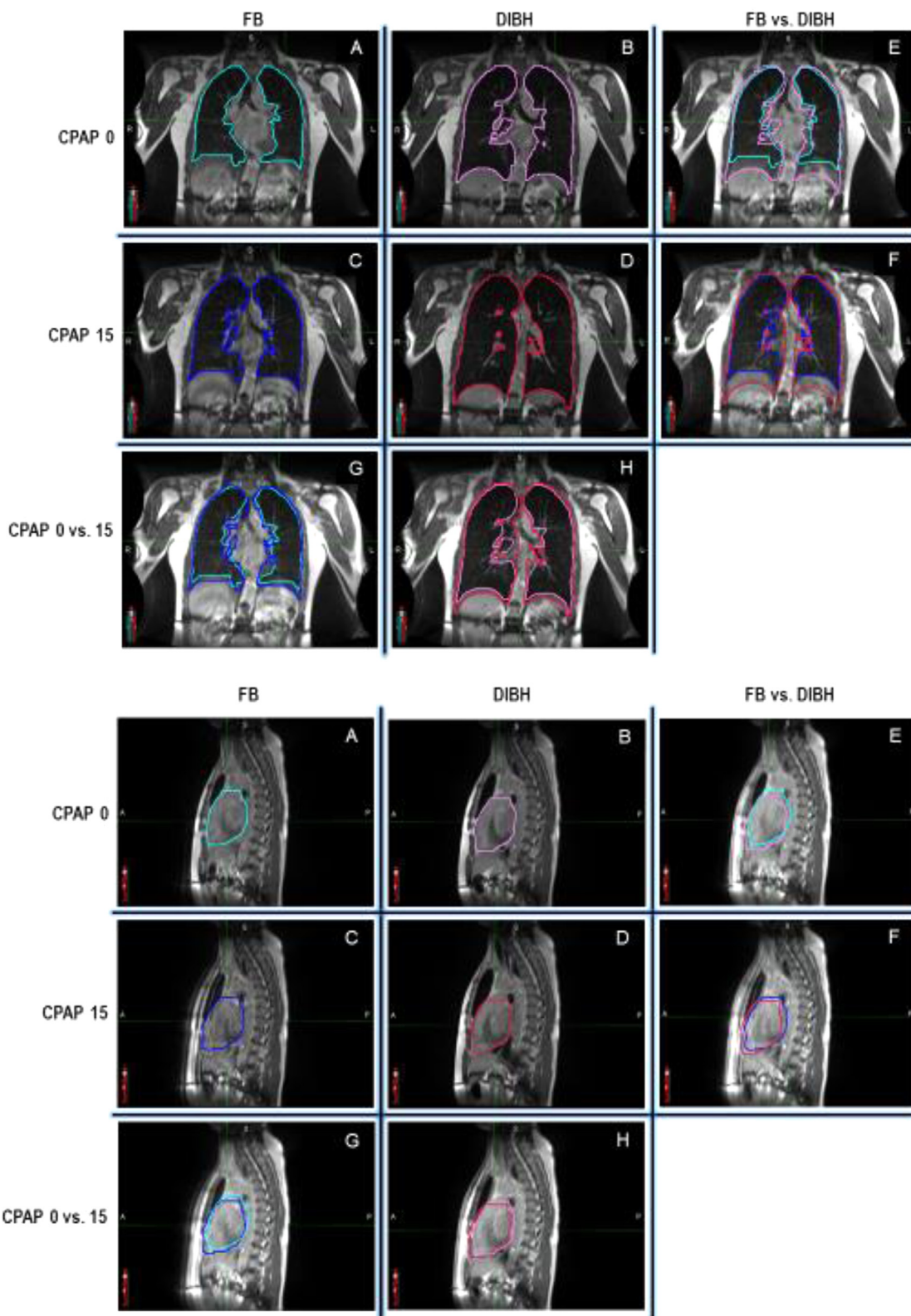
Figure 2　Low-field magnetic resonance images from a healthy volunteer illustrating the effect of continuous positive airway pressure (CPAP) on lung and heart positioning. **(A)** The lung and heart under free breathing (FB) conditions (FB-0 cm H_2O). **(B)** A deep inspiratory breath hold (DIBH) without positive airway pressure (DIBH-0 cm H_2O). Similarly, **(C)** shows FB-15 cm H_2O and **(D)** shows DIBH-15 cm H_2O. The color-coded overlay images **(E, F, G, H)** demonstrate direct comparisons in lung and heart volumes when applying CPAP pressures (between 0 cm H_2O and 15 cm H_2O) and breath-hold state (FB or DIBH), highlighting the increased lung volumes and inferior heart shift.

Table 2 Cardiothoracic anatomic geometry measurements under different respiratory management techniques

N = 6	FB-0 cm H$_2$O mean (SD)	FB-6 cm H$_2$O mean (SD)	FB-10 cm H$_2$O mean (SD)	FB-12 cm H$_2$O mean (SD)	FB-15 cm H$_2$O mean (SD)	DIBH-0 cm H$_2$O mean (SD)	DIBH-6 cm H$_2$O mean (SD)	DIBH-10 cm H$_2$O mean (SD)	DIBH-12 cm H$_2$O mean (SD)	DIBH-15 cm H$_2$O mean (SD)
Lung volume (cc)	2671 (582)	3091 (821)	3437 (816)	3583 (948)	3849 (974)	5278 (253)	5874 (372)	5715 (361)	5831 (435)	5936 (408)
% Δ lung volume	ref.	14% (18%)	29% (23%)*	34% (23%)*	44% (27%)†	105% (45%)*	129% (52%)†	123% (53%)†	126% (47%)†	131% (51%)†
Heart volume (cc)	763 (82)	769 (134)	757 (132)	729 (129)	707 (134)	729 (97)	678 (53)	660 (93)	668 (89)	664 (98)
% Δ heart volume	ref.	1% (10%)	−1% (10%)	−2% (9%)	−5% (9%)	−4% (7%)	−11% (7%)	−12% (7%)*	−12% (7%)*	−12% (9%)*
Heart shift‡										
Lateral (cm)	ref.	−0.02 (1.35)	−0.28 (1.58)	−0.27 (1.69)	−0.38 (1.71)	−0.46 (1.50)	−0.11 (1.21)	−0.28 (1.50)	−0.58 (1.49)	−0.55 (1.50)
Anterior/posterior (cm)	ref.	−0.38 (1.00)*	−0.34 (1.41)*	−0.28 (1.20)	−0.51 (1.19)*	−1.19 (1.53)†	−1.61 (1.39)†	−1.42 (1.61)†	−1.54 (1.48)†	−1.59 (1.41)†
Superior/inferior (cm)	ref.	−0.57 (0.59)	−0.86 (0.53)*	−0.96 (0.54)†	−1.18 (0.71)†	−1.94 (0.56)†	−1.97 (0.60)†	−2.08 (0.58)†	−2.11 (0.61)†	−2.18 (0.59)†

Abbreviations: DIBH = deep inspiratory breath hold; FB = free breathing; ref. = reference.
* Indicates $P < .05$.
† Indicates $P < .01$.
‡ Shift in location of heart relative to position of heart centroid at reference condition. Positive values defined as left, superior, and superior shifts.
Pressures delivered with continuous positive airway pressure (CPAP). Student 2-tailed paired t tests compared with reference condition (FB at CPAP 0 cm H$_2$O).

heart volumes decreased by 12% (standard deviation [SD] 7%, $P < .01$), 12% (SD 7%, $P = .01$), and 12% (SD 9%, $P = .01$), respectively.

Inferior and posterior displacements of the heart were observed without significant shift in the medial or lateral axis. This information is also summarized in Table 2 with significance relative to reference FB-0 cm H$_2$O shown. Comparing FB-15 cm H$_2$O to DIBH-0 cm H$_2$O, DIBH trended toward greater magnitude shifts, although only significantly in the posterior direction and not in the inferior direction (mean shift posterior 0.51 cm vs 1.19 cm, $P = .05$; mean shift inferior 1.18 cm vs 1.94 cm, $P = .11$). The addition of pressure in DIBH-15 cm H$_2$O had the greatest effect on the heart position and was significantly greater than DIBH-0 cm H$_2$O (mean shift posterior 1.59 cm vs 1.19 cm, $P = .03$; mean shift inferior 2.18 cm vs 1.94 cm, $P = .20$).

Table 3 best summarizes the differences in repeated lung volumes with varied pressures. Of note, the lung volumes of 2 consecutive breath holds were more consistent with CPAP DIBH-15 cm H$_2$O (mean difference 69 cm^3, ICC = 0.97) than at DIBH-0 cm H$_2$O (mean difference 408 cm^3, ICC = 0.00). No change in heart position repeatability was seen, with mean heart superior-inferior centroid location differences of <1.5 mm across the cohort.

Table 4 lists the consensus motion artifact scores assigned to each set of images. No motion artifact was seen for any of the breath hold images, with all images scoring 0, which was significantly different from the reference condition (mean artifact score of 1.83). As expected, adding substantial CPAP pressure (15 cm H$_2$O) yielded a statistically significant difference from baseline free breathing conditions ($P = .03$).

Discussion

In the present study, we showed the compatibility of using CPAP for potential applications on an MR-guided radiation treatment (MRgRT) machine. Unlike previous studies that compared FB images with CPAP at one set pressure, one distinct benefit of our study is that by implementing MRI, we had the ability to study varying levels of pressure relative to free breathing and breath hold alone, as well as the potential use of CPAP-aided DIBH. Overall, the approach was well-tolerated, with participants getting more acclimated to the airway pressure after the imaging session. Increased CPAP pressures predictably increased lung volumes and shifted the heart inferiorly and posteriorly. However, implementing CPAP alone led to anatomic shifts that were smaller in magnitude, less lung volume increase, and resulted in images with more motion artifact compared with DIBH alone. This suggests that CPAP in a FB setting may not be as robust for use in MRgRT and may not be a suitable substitute for DIBH. Nevertheless, for patients who are unable to tolerate a breath-hold,

Table 3   Reproducibility of anatomic changes in consecutive breath holds under different CPAP-applied pressures

N = 6	0 cm H_2O	6 cm H_2O	10 cm H_2O	12 cm H_2O	15 cm H_2O
Mean absolute Δ lung volume (SD), cc	408 (392)	198 (126)	321 (169)	126 (136)	69 (70)
Correlation coefficient* (95% CI)	0.00 (0.00-0.00)	0.78 (0.27-0.97)	0.57 (0.13-0.92)	0.91 (0.61-0.98)	0.97 (0.87-0.99)
Mean absolute sup/inf heart shift (SD), cm	0.13 (0.12)	0.12 (0.06)	0.12 (0.09)	0.14 (0.09)	0.11 (0.06)
Correlation coefficient* (95% CI)	0.95 (0.77-0.99)	0.97 (0.81-1.00)	0.96 (0.83-0.99)	0.96 (0.82-0.99)	0.97 (0.87-0.99)

Abbreviations: CI = confidence interval; CPAP = continuous positive airway pressure; SD = standard deviation; sup/inf = superior/inferior.
* Intraclass correlation coefficient, where 0 signifies no reliability between repeated measurements and 1 signifies perfect reliability.

CPAP coupled with FB may provide some cardioprotection, as evidenced by favorable centroid shifts compared with FB alone. The combination of CPAP-aided DIBH led to the greatest degree of lung volume expansion and inferior or posterior shift of the heart. More importantly, the reproducibility results showed that CPAP-aided DIBH yielded more consistent lung volumes, suggesting potential for improving the reproducibility of breath holds.

Several published studies under CT imaging conditions have examined the role of CPAP use during radiation treatment planning and delivery. A pilot study by Goldstein et al looking at stereotactic body radiation therapy (SBRT) for lung tumors under 8 to 15 cm H_2O CPAP showed a relative lung volume increase of 32% compared with standard FB.[20] Two clinical trials of women receiving left-sided breast radiation therapy highlighted that implementing CPAP led to increases of total lung volume by 35% and 60%, achieved with 8 to 15 cm H_2O and 20 cm H_2O, respectively.[24,27] One previous study of SBRT patients showed a lesser degree of 8% lung volume increase.[23] The authors of this study partly attribute the decreased volume increase to the CPAP pressure (average 6.9 cm H_2O) being less than the pressures in other studies. Our study corroborates this explanation, with no statistically significant lung volume increase seen with FB-6 cm H_2O and a 44% lung volume increase seen with FB-15 cm

H_2O. This also suggests that for CPAP to be beneficial in this setting, ample pressure must be provided, although these settings may depend on overall tolerability of the pressure settings. However, we saw an even greater magnitude of lung volume increase to 105% above baseline with breath hold alone and 131% above baseline with DIBH-15 cm H_2O. This finding was also shown in another recent study investigating the combination of DIBH + CPAP, with lung volume increase of about 100% with DIBH at 15 cm H_2O.[28]

Decrease in heart volume and posteroinferior heart displacement are additional benefits seen with the application of CPAP. In the previous reported clinical experiences with CPAP, a minimal average 26 cm^3 decrease was seen in one study, and no heart volume difference was seen in another.[20,27] We similarly did not see any significant change in heart volume with CPAP alone. However, with DIBH in conjunction with CPAP, we were able to see a 12% decrease in heart volume at DIBH-15 cm H_2O. The other DIBH + CPAP study showed a 9.5% decrease in heart volume at this condition. In addition, our study looked at the shift in the heart centroid relative to the centroid at the free breathing condition, and we saw posterior and inferior shifts associated with application of CPAP, greater shifts associated with DIBH, and the greatest shifts with the combination.

Table 4   Image artifact scores

Participant (N = 6)	FB-0 cm H_2O	FB-6 cm H_2O	FB-10 cm H_2O	FB-12 cm H_2O	FB-15 cm H_2O	DIBH-0 cm H_2O	DIBH-6 cm H_2O	DIBH-10 cm H_2O	DIBH-12 cm H_2O	DIBH-15 cm H_2O
1	1	1	1	2	1	0	0	0	0	0
2	2	N/A	2	1	2	0	N/A	0	0	0
3	2	N/A	1	1	1	0	N/A	0	0	0
4	2	2	2	1	1	0	0	0	0	0
5	2	1	1	1	1	0	0	0	0	0
6	2	1	1	1	1	0	0	0	0	0
Mean	1.83	1.25	1.33	1.17	1.17	0	0	0	0	0
t Test *P* value	ref.	0.18	0.08	0.10	0.03	<0.01	<0.01	<0.01	<0.01	<0.01

Abbreviations: DIBH = deep inspiratory breath hold; FB = free breathing; N/A = not available.
Pressures delivered with continuous positive airway pressure. Scores were defined to the blinded graders as 0: no motion artifact; 1: minor motion artifact; 2: major motion artifact. Deep inspiratory breath hold scores were obtained by averaging the scores from the first trial and second trial.

In the clinical setting, other studies have shown the clinical benefits of these geometric changes. Improvement in lung dose and heart dose parameters was demonstrated in these experiences,[20,24,27,28] highlighting future opportunities to quantify the dosimetric benefits of CPAP-guided MRgRT. In the case of SBRT treatment of lung tumors, the planned target volumes were decreased by 19% to 24% with administration of CPAP.[20,29] Another notable takeaway in one study was that radiation therapy with CPAP did not increase treatment setup time compared with free-breathing setup, and the authors concluded CPAP may be a viable option for respiratory management in resource-limited radiation oncology centers.[24] Another clinical question that arises is the viability of CPAP in the population of patients with thoracic malignancies who often have underlying pulmonary comorbidities. In the case of chronic obstructive pulmonary disease, use of CPAP has been shown in a prospective trial to increase 5-year survival among patients with both chronic obstructive pulmonary disease and concurrent obstructive sleep apnea.[30] In one prospective trial with 40 patients investigating CPAP for treatment of lung tumors, left-sided breast cancer, or liver metastases, 10 of the patients had underlying chronic obstructive pulmonary disease as well. The volumetric benefits of CPAP were also seen in this subgroup.[29]

MRgRT is an evolving technology which can provide real-time direct visualization of tumors and superior soft tissue delineation capabilities. It has been used in the clinical setting with intracranial, head and neck, lung, abdominal, and pelvic tumors, allowing for decreased setup margins and the potential for decreased normal tissue toxicity.[31] For abdominal and pelvic tumors, it may help patients avoid potential complications with placement of fiducial markers that would otherwise be necessary for safe delivery of radiation. In our study, we show that CPAP is a tool that could be implemented in the MRgRT setting. Although MRgRT is typically located in resource-rich centers, there may still be a role for CPAP. Our study showed less motion artifact with the addition of CPAP and more consistent lung volumes with higher CPAP settings. This may be due to the need for less force applied by the diaphragm with the pressure support of the CPAP machine and thus, less patient fatigue. More reproducible holds offer the possibility of shorter treatment times associated with gated radiation therapy, which can be explored in future work. Reckhow et al described their experience with patients who had difficulty tolerating DIBH alone were able to endure CPAP-aided DIBH.[28] Although the CPAP-aided DIBH did significantly reduce mean heart dose and mean lung dose more than DIBH alone, the authors also hypothesized that adding CPAP to DIBH could reduce the respiratory effort needed by patients for DIBH. Patient compliance with MRgRT sessions frequently depends on the ability to reliably reproduce breath holds, and these studies suggest that CPAP could be worthy of further investigation as an MR-compatible breath hold aid. It would represent a potential way to safely treat patients with intrathoracic or upper abdominal tumors who would not otherwise be candidates for MRgRT due to poor tolerability of DIBH.

CPAP is not the only respiratory approach that has been considered for facilitating breath holds in the radiation therapy setting. Other studies have looked at the use of mechanical ventilation for both more controlled breathing patterns and more sustained breath holds.[32,33] One such study revealed breath holds with mean duration time of 6 minutes with preparatory mechanical hyperventilation before breath hold. Another approach is to use high frequency ventilatory strategies occasionally used in the intensive care unit as a way to oxygenate patients without causing much diaphragmatic movement. One series of publications described a technique for limiting liver tumor movement to 3 mm in the setting of single-dose SBRT treatments with the aid of high frequency jet ventilation and gold marker fiducials.[34,35] High frequency percussive ventilation has also been used to create sustained breath holds, with rapid (300-600 breath/min) percussive breaths helping to oxygenate patients during breath holds of 5 to 11 minutes.[36,37] One retrospective study described the effect of using high frequency percussive ventilation in the treatment of thoracic Hodgkin lymphoma and showed a decrease in cardiac dose.[38] Although these breath hold durations offer strong potential, these respiratory interventions are much less widespread than CPAP and have thus far been mostly limited to investigational settings.

The present study does have clear limitations in its small sample set of healthy participants. However, using each participant as their own control, allowed accurate characterization of geometric changes after CPAP. Each participant was able to reliably perform coached DIBH, and when in practice, the combination CPAP-aided DIBH approach may be more relevant for those patients who are borderline candidates for DIBH who would otherwise be ineligible due to fatigue and reproducibility limitations. Reproducibility was based on 2 consecutive breath holds, whereas a typical fraction of radiation can require 7 to 9 DIBHs of 20 seconds each.[39] In addition, this study only looked at intrafraction repeatability, whereas interfractional changes in body positioning and target position are also of great relevance. Future studies may include assessment of breath hold duration with and without CPAP in the treatment position and of tolerability in a clinical patient population less able to maintain DIBH.

Conclusion

In this initial feasibility study, integrating CPAP into an MR-linac for healthy volunteers demonstrated increasing heart displacement and lung volume as well as decreased associated image artifact. CPAP-aided DIBH also resulted

in geometric changes of greater magnitude, and less volume difference between consecutive breath holds. Overall, CPAP was found to be compatible with the MR-guided radiation treatment clinical environment and was well-tolerated by the volunteer cohort. With confirmation of these findings in a larger patient cohort, clinical effectiveness can be further evaluated.

Acknowledgments

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