

Advantage of using deep inspiration breath hold with active breathing control and image-guided radiation therapy for patients treated with lung cancers

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Abstract

Purpose: The aim of this study was to evaluate the irradiated volume and doses to the target, heart, left lung, right lung and spinal cord, the number of segments and treatment time by using moderated deep inspiration breath hold (mDIBH) with active breathing control (ABC) and image-guided radiotherapy (IGRT) for patients treated with lung cancers. **Methods:** The suitability of this technique for lung patient treated with ABC was investigated and the solutions to achieve better treatments were discussed. Eleven lung cancer patients (3 left-sided and 8 right sided lesions) with stages I-III underwent standard free breath (FB) and ABC computed tomography (CT) scans in the treatment supine position. This can be achieved by applying respiratory manoeuvres, such as mDIBH, during which the threshold volume utilized is defined as 75-80% of the maximum inspiratory capacity. Five to seven, 6-MV photon beams with optimized gantry angles were designed according to the tumor location to conform to the PTV while sparing as much heart, spinal cord, and contra lateral lung as possible. For eleven patients, treatment planning using mDIBH CT data with intensity modulated radiation therapy (IMRT) was then reoptimized on the free breathing data set for comparison. The studied parameters of the plans for each patient were evaluated based on the average of the minimum, mean, and maximum difference in dose, the range of difference, and the *p*-value using two-tailed paired *t* test assuming equal variance. **Results:** The average volume of the planning target volume (PTV) in 11 patients increased to 1.32% in ABC compared to FB. The average volume of heart in 11 patients decreased to 2.9% in ABC compared to free breathing IMRT. In the case of lungs, the volume increased to 27.5% and 25.85% for left and right lungs, respectively. The range of mean difference in dose to the PTV in 11 patients was -54 cGy to 230 cGy with ABC technique when compared with free breathing. The range of mean dose difference of heart in 11 patients observed were -88 cGy to 66 cGy ($p < 0.0410$) between ABC and FB. The range of maximum dose difference to the spinal cord in 11 patients were -1592 cGy to 190 cGy ($p < 0.041$) with ABC technique when compared with FB IMRT. Monitor units (MUs) were -22.9% less in ABC compared to FB. Segments were more in ABC compared to FB for about 16.39% on an average. The average of minimum, mean and maximum difference in dose to the right lung and left lung were less in ABC compared with FB. **Conclusion:** In most of the cases, IGRT with ABC significantly reduces the mean dose to heart, right lung, left lung, and spinal cord compared with FB. Discrepancy observed in few cases made the statistical data inconsistent. Depending on anatomy and arbitrary phase of the breathing cycle, the results may vary and for better outcome of the results optimum treatment procedures need to follow.

Keywords: Active breath control; mDIBH; Lung tumors

Introduction

Treatment modalities for the lung cancers in radiation oncology field are rapidly evolving. More than 60% of patients with lung cancers undergoing radiation therapy (RT) during the course of their disease, 45% for initial treatment and 17% for palliation.¹⁻² Understanding the normal anatomy is very important for delineating the tumour. Abnormal and doubt-

ful structures should be evaluated for fluid content to exclude pericardial fluid in a recess.³⁻⁴ For better delineating the target and normal structures computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) were used together. It is also now possible to do 2D-2D match and 3D-3D match with the help of electronic portal

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imaging device (EPID) and cone beam CT (X-Ray volume imaging (XVI)) respectively to measure and account for interfraction variations. In motion management intrafraction variation is also one of the important factors to account.

Intrafraction motion is caused by (a) respiratory (b) skeletal-muscular, (c) cardiac, and (d) gastrointestinal systems. The problems of respiratory motion during radiotherapy are image-acquisition limitations, treatment-planning limitations and radiation-delivery limitations. Methods to account for respiratory motion in radiotherapy⁵ are

- motion-encompassing methods,
- respiratory gating methods,
- breath-hold methods,
- forced shallow breathing with abdominal compression, and
- real-time tumor-tracking methods.

In our study active breathing control (ABC) was used which is under breath-hold method. The purpose of this study is to investigate the impact of using ABC treatment with moderated deep inspiration breath hold (mDIBH) on the PTV, lungs, heart, and spinal cord. Dose to the PTV and critical structures, volume of organs, treatment time, number of segments and monitor units were compared in free breath (FB) to ABC. This procedure helps us to check the suitability of ABC technique to any lung patient. In case of contrary results the solutions to achieve the better results are also given.

Methods and Materials

One of the main benefits of the active breathing coordinator⁶⁻⁸ is that it is useful for tumor immobilization. Eleven lung cancer patients (3 left-sided and 8 right-sided lesions) with Stages I-III underwent standard FB and ABC CT scans in the treatment position. Among eleven patients, four are female and seven are male with age from 30 to 82 years. Sixteen slice Siemens Somatom CT scanner was used to scan 2 mm slices at the predefined threshold level. This can be achieved by applying respiratory manoeuvres, such as mDIBH, during which the threshold volume utilized is defined as 75-80% of the maximum aspiratory capacity. Applying mDIBH technique increases the total volume of the lungs, moving the chest wall anterior and the diaphragm inferior. For patient set-up, we used all-in-one (AIO) (Orfit, Jericho, New York, USA) immobilization system and Vac-Lok hemibody cast (MED-TEC, Orange City, IA, USA). Patients with immobilization and ABC underwent CT simulation. Images with moderate mDIBH from CT were sent to three-dimensional (3D) XiO treatment planning system (TPS) (CMS Inc., St. Louis, MO, USA) through DICOM 3.0 Network.

The clinical target volume (CTV) and planning target volume (PTV) were derived by applying 8 mm and 7 mm margin to gross tumor volume (GTV) and CTV, respectively.

Additional 5 mm margin was outlined to include the shift in tumor position during ABC gating.⁹⁻¹⁰ Fused magnetic resonance imaging (MRI) and position emission tomography (PET) CT images were used for delineation of the target structures. Simultaneously, contouring was done on FB images also. Five to seven 6-MV photon beams with suitable gantry angles were designed¹¹⁻¹³ (**Figure 1**) according to the tumor location to conform to the PTV while sparing as much heart, spinal cord, and contra lateral lung as possible. Additionally, transverse CT slices and digitally reconstructed radiographs (DRR) from the BEV were used to optimize field placement. Planning for 5000 cGy in 10 fractions was done using step and shoot IMRT technique (Elekta Synergy linear accelerator) with 1 cm segment size and maximum intensity levels of 10. The segmented beam data was sent to the machine console for treatment.

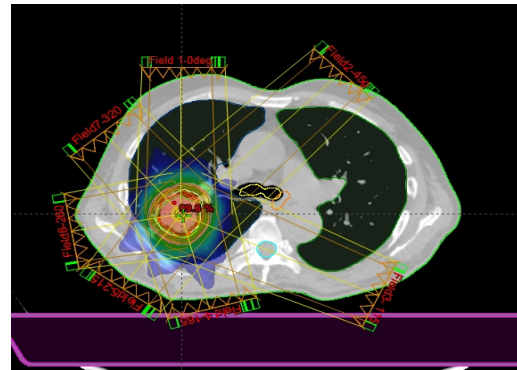


FIG. 1: Beam placement in lung cases in sagittal transverse view.

For eleven patients, treatment planning using mDIBH CT data with IMRT was then reoptimized on the free breathing data set for comparison with the same plan that was used for ABC. Dose-volume histograms for the PTV, heart, right lung, left lung, and spinal cord were analyzed. The studied parameters of the different plans for each patient were evaluated based on the minimum, mean and maximum difference, the range of difference, and the *p* value using two-tailed paired *t* test assuming equal variance.¹⁴ The change in volumes of PTV, lungs, heart and spinal cord were recorded. In addition, the PTV volume receiving at least 95% of the prescription dose (V_{95}) and 105% of the prescription dose (V_{105}), ipsilateral and contra lateral lungs volume receiving at least 20 Gy (V_{20}), heart volume receiving more than 30 Gy (V_{30}), spinal cord maximum dose and absolute volume receiving more than 45 Gy (V_{45}), the number of monitor units (MUs) and segments were compared between FB and ABC for a single fraction of 5 Gy.

Results

Analysis of volume and dose in ABC and FB

PTV

The average volume of the PTV in 11 patients increased to 1.32% in ABC compared to FB with the range of difference is

from -33.9% to 22.29% ($p < 0.2536$) as shown in **Figure 2**. Maximum difference and minimum differences were -33.9% (-19.13 cc) and -0.70% (-2.3 cc), respectively. The range of mean difference in dose to the PTV in 11 patients was -54 cGy to 230 cGy ($p < 0.5447$) with ABC technique when compared with FB IMRT. The average of minimum, mean and maximum differences in dose to the PTV were -222.45 cGy ($p < 0.2889$), 14.09 cGy ($p < 0.5447$) and 33.6 cGy ($p < 0.5268$) respectively. The range of minimum difference in dose was from -2002 cGy to 407 cGy and the range of maximum difference in dose was from -280 cGy to 430 cGy. The minimum, maximum and mean dose to the PTV in both FB and ABC are shown in **Table 1**. The V_{95} and V_{105} of the PTV were analyzed in both ABC and FB techniques as shown in **Figure 3**. The mean difference of PTV volume receiving 95% and 105% of dose are from 0% to -10% ($p < 0.00815$) and 26% cc to -82% cc ($p < 0.211$) respectively.

The average volumes of heart in 11 patients decreased to -18.83% in ABC compared to free breathing with the range of difference is from -49.46% to 25.31% ($p < 0.4191$). The maximum and minimum differences were observed -54.51% (-183.51 cc) and -2.9% (-12.73 cc) respectively. Volume comparisons for heart were illustrated in **Figure 2**. The range of mean dose difference in 11 patients observed was -88 cGy to 66 cGy ($p < 0.0410$) between ABC and FB. The average of minimum, mean and maximum difference in dose to the heart are -13.34 cGy ($p < 0.2783$), -89.2 cGy ($p < 0.0410$) and -385 cGy ($p < 0.1366$) respectively. The range of minimum difference was from -129 cGy to 2 cGy and the range of maximum difference is from -1847 cGy to 1124 cGy. The minimum, maximum and mean dose to the Heart in both FB and ABC were shown in **Table 1**. Amount of heart receiving more than 30 Gy (V_{30}) were analyzed in both ABC and FB techniques and shown in **Figure 3**. The mean difference of heart volume receiving more than 35 Gy of the dose are from 1.68 cc to -16.53 cc ($p < 0.2765$).

Heart

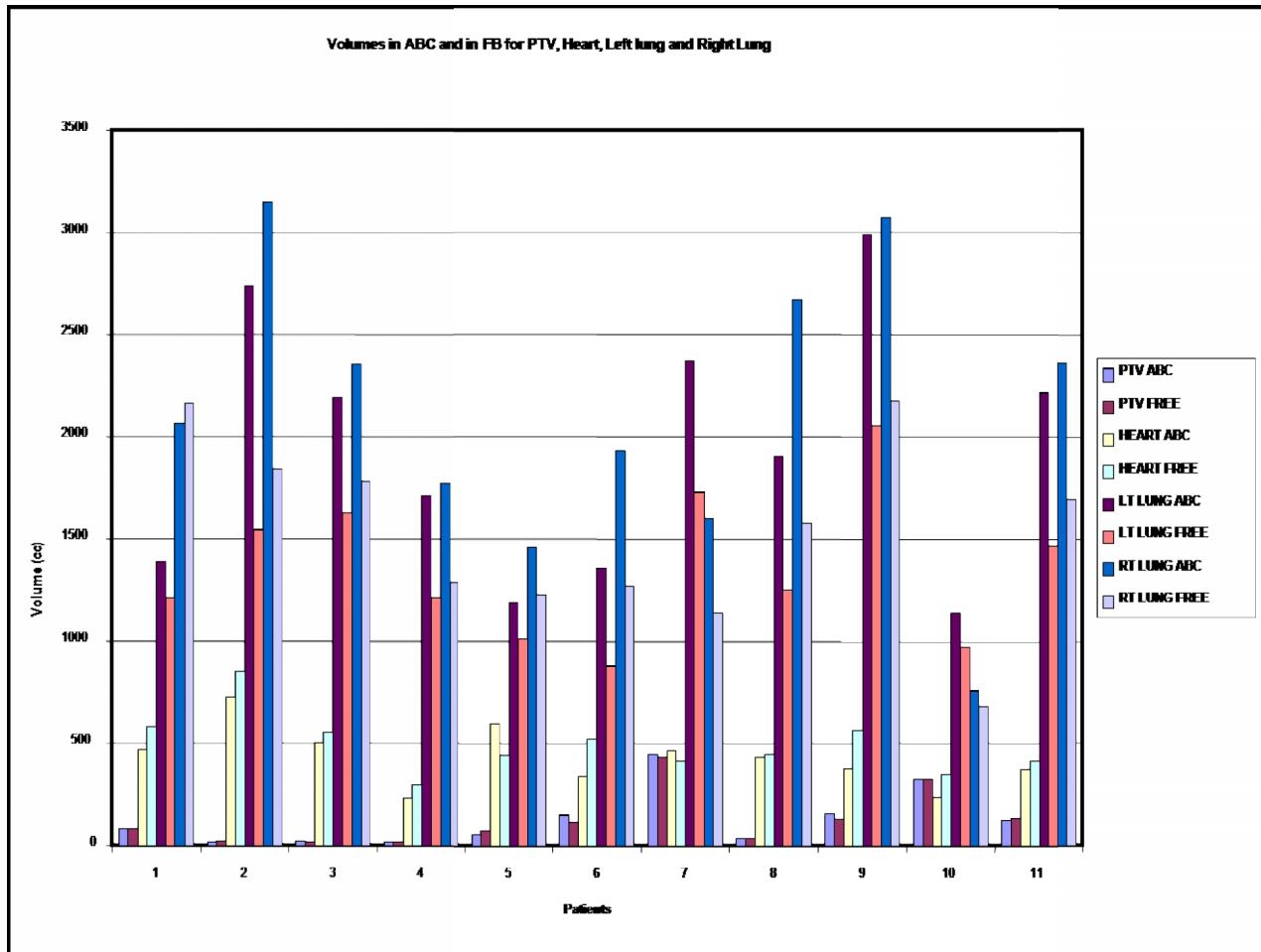


FIG. 2: Comparison of volumes in ABC with FB for PTV, heart, left lung, right lung.

TABLE 1: Minimum, maximum and mean dose (cGy) to the PTV and critical structures in FB and ABC for 11 Patients.

#	PTV ABC			PTV Free			Heart ABC			Heart free			RT Lung ABC			RT Lung free			LT Lung ABC			LT Lung FB			Spinal cord ABC	Spinal cord FB		
	Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)			Dose (cGy)	Dose (cGy)		
	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	max
1	4479	5215	5035	4786	5203	5059	1	1722	125	1	543	45	0	349	146	0	782	162	0	5002	884	0	5203	1038	1585	1541		
2	3336	3708	3595	3384	3597	3598	0	0	0	0	19.6	0	0	5160	250.6	0	5236	347.2	0	1120	82.6	0	1048	119	1493	1513		
3	4623	5206	5030	4774	5201	5035	0	667	25	0	1333	113	0	5027	267	0	5083	366	0	969	94	0	979	108	1435	1450		
4	4553	5183	5061	4565	5165	5029	5	850	157	3	714	91	0	5127	556	0	5161	671	0	633	74	0	511	65	332	564		
5	4067	5445	4981	4198	5329	4937	28	4130	772	32	2834	703	5	5312	1262	1	5322	1241	1	1593	261	1	1624	285	2867	2769		
6	4830	5520	5270	4700	5190	5040	20	3740	290	20	4740	500	0	3430	240	0	2450	268	0	5650	1620	10	5170	1640	1580	2070		
7	1943	5749	5004	3945	6029	5023	214	4638	1347	343	5002	1420	15	5362	1293	25	6029	1893	16	3839	745	25	4646	787	3284	4723		
8	3994	5323	4933	4467	5198	5047	0	3	0	0	19	2	0	5091	314	0	5236	544	0	2043	172	0	2141	263	3023	4615		
9	3391	5254	5015	4469	5342	5019	0	62	14	0	83	20	0	2421	268	0	2896	210	0	5357	740	0	5404	1223	2092	1892		
10	4391	5262	5037	4346	5230	5044	37	2843	262	39	4690	522	14	5253	1984	23	5239	2908	4	3875	509	11	4718	574	4205	4859		
11	3437	4210	4024	3080	4197	4037	10	4790	253	24	5112	586.3	0	4976	906.3	5	5248	1807	0	1743	293	5	1867	416	1201	1295		

= Patient Number

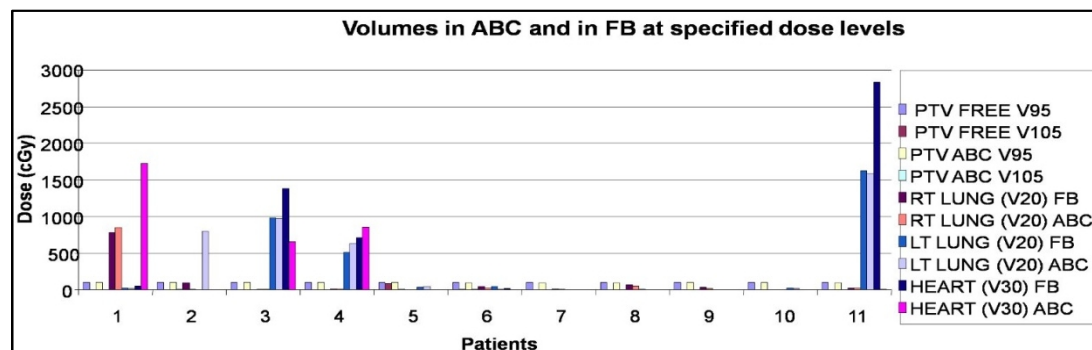


FIG. 3: V₉₅ and V₁₀₅ of PTV, V₃₀ of heart, V₂₀ of left lung and right lung volumes in FB and mDIBH ABC.

Left lung

The average volumes of Left lung (after deducting the PTV volume in that particular lung) in 11 patients increased to 27.5 % in ABC compared to free breathing with the range of difference is from 12.66% to 43.44 % ($p < 0.000168$). Maximum difference and minimum differences were 43.44 % (1190 cc) and 12.66 % (176 cc), respectively. The comparison of left lung volume is shown in **Figure 2**.

The range of mean dose difference to the left lung in 11 patients were -483 cGy to 9 cGy ($p < 0.1824$) with ABC technique when compared with free breathing IMRT. The average of minimum, mean and maximum difference in dose to the left lung are -2.8 cGy ($p < 0.0455$), -94.9 cGy ($p < 0.1824$) and -135.6 cGy ($p < 0.4266$) respectively. The range of minimum difference was from -10 cGy to 0 cGy, and the range of maximum difference was from -843 cGy to 480 cGy. The minimum, maximum and mean dose to the left lung in both FB and ABC are shown in **Table 1**. The V_{20} of left lung was analyzed in both ABC and FB techniques and shown in **Figure 3**. The mean difference of left lung volume receiving more than 20 Gy of the dose were from -6.5 % to -92 % ($p < 0.0927$).

Right Lung

The average volumes of right lung (after deducting the PTV volume in that particular lung) in 11 patients increased to 25.85% (594.5 cc) in ABC compared to free breathing with the range of difference is from 41.33% cc to 4.62% ($p < 0.001039$). The maximum and minimum differences were 41.33% (1301 cc) and 4.62% (100.29 cc), respectively. The comparison of right lung volume in FB and ABC is shown in **Figure 2**.

The range of mean difference in dose to the right lung in 11 patients were -924cGy to 58cGy ($p < 0.0368$) with ABC technique when compared with free breathing IMRT. The average of minimum, mean and maximum difference in dose to the right lung are (-1.8cGy) ($p < 0.1918$), -264.6 cGy ($p < 0.0368$) and -8843 cGy ($p < 0.3519$), respectively. The range of minimum difference was from -10 cGy to 0 cGy and the range of maximum difference was from -667 cGy to 680 cGy. The minimum, maximum and mean dose to the right lung in both FB and ABC are shown in **Table 1**. The V_{20} of right lung was analyzed in both ABC and FB techniques and shown in **Figure 3**. The mean difference of right lung volume receiving more than 20 Gy of the dose was from 1% to -98 % ($p < 0.24556$).

Spinal cord

The range of maximum dose difference to the spinal cord in 11 patients were -1592 cGy to 190 cGy with ABC technique when compared with free breathing IMRT. The average of maximum difference in dose to the spinal cord was -382.18 cGy ($p < 0.1366$) as shown in **Table 1**. The V_{45} of spinal cord

was analyzed in both ABC and FB Techniques. The mean difference of spinal cord volume receiving more than 45 Gy was from 0.2 cc to 0.59 cc ($p < 0.1394$), and out of 11 cases only one patient received more than 5 cc of spinal cord.

MUs and segments comparison

The number of MUs was less with ABC treatment compared with FB in all 11 lung patients (**Figure 4**). The mean % of variation was -22.9%, the maximum % of variation was -66.4%, and the minimum % of variation was 0.497%, whereas the difference in mean % variation was 12.46% ($p < 0.0589$). Out of eleven patients only one patient result shown negative with more number of monitor units compared to FB. It was found that more number of segments were required in ABC compared to FB (**Figure 5**). The minimum, maximum, and mean % variation were 0%, 16.39% and 58.22%, respectively. The mean difference in % variation was 23.10 % ($p < 0.0186$).

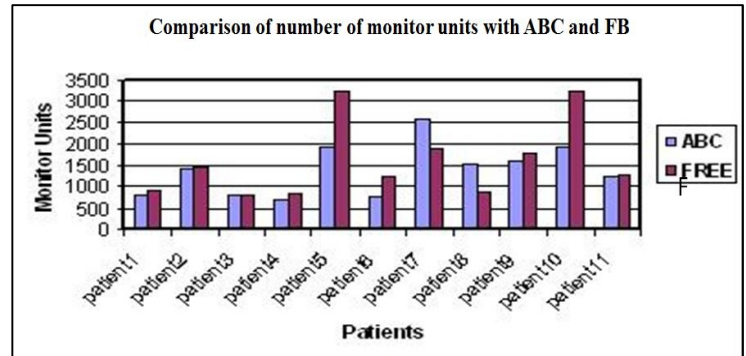


FIG. 4: Comparison of number of monitor units (MUs) in ABC and FB.

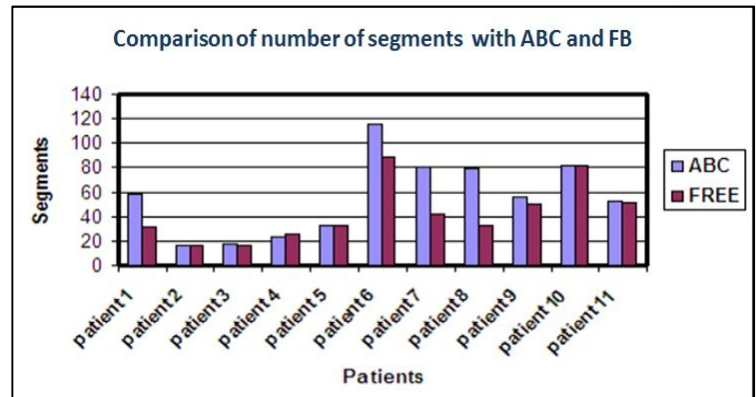


FIG. 5: Comparison of number of segments with ABC and free breath.

Discussion

The present study explores improvement achieved by the mDIBH if it is based on ABC with mDIBH rather than free breathing CT scan using identical treatment plan parameters. It is acknowledged that the free breathing scan represents

only one arbitrarily selected state of the patient. This result in the inconsistency of data (for example, in two patients the heart dose decreases in the free breathing based plan).

The mDIBH significantly reduced the heart, lung, and spinal cord doses compared with FB, while maintaining excellent coverage of the PTV. However, the advantages of mDIBH compared with the FB technique depend on few factors such as patient breathing capacity, anatomy, dose rate of the machine, etc.

Patient selection is also one of the important factors. An old person who cannot perform breath control and a young child who cannot understand the procedure are not ideal patients for the treatment. In reality the free breathing scans cannot be taken at a predefined phase. In fact, scans at some particular phase are taken even during the free breathing. If all the free breathing scans are done in inspiration in the same phase where ABC has been done, we may not see the much difference between both approaches. Due to this reason, we have taken 11 patients for this study. The randomness of the free breathing scan needs to be analyzed. But with ABC, we are certain about the phase in which the treatment will be delivered.

With high dose rate machines the treatment time will come down, which is very much useful to perform ABC. Anatomy is also very important factor. As each patient is having unique structure the statistical data that was obtained in few cases were insignificant. In few cases where mDIBH have no significant effect and are with contradict results, those patients with other threshold or phase of the treatment should be taken for analysis to get the optimal phase of the treatment. Because of increased space between the other organs at risk and the PTV during particular phase of the breathing cycle, the target coverage and protection to OAR's can be achieved. The use of mDIBH with ABC produced no significant difference in PTV volume for (V_{95}) and (V_{105}). ABC reduced the number of MUs and increased the segments.

In the present study, the average mean heart dose for 11 patients decreased to 76.3%. This is a significant result. But in

two cases, it showed the maximum dose in ABC is more compared to FB. This necessitates further study on gating. During gating, treatment will be delivered in some particular phase only. There is a need to check the suitability of the phase to the ideal treatment. The best phase of the treatment is the phase where critical structures should be as far away from the target as possible in the beams eye view of the beam in the treatment planning. Because of this at least few phases should be thoroughly analyzed instead of going for treatment with gating. **Figure 6** shows the different phases on full cycle of breathing.

As demonstrated in **Figure 3**, the impact of mDIBH on heart calculations shows good results as observed with heart V_{30} values. However, because the dose reduction with mDIBH occurs primarily in the anterior part of the heart where the coronary vessels are positioned, significantly greater benefits in reducing long-term ischemic disease might be expected. But, we can see the discrepancy for two patients who are getting more volume (V_{30}) in ABC compared with FB. This is the interesting area in the present paper, and we need more attention to avoid such negative results that may happen with any gating method.

Margin reduction can be achieved by taking into account the breathing motion and setup errors. The margin will vary for each and individual patient. This information is very useful for adaptive radiation therapy.¹⁵⁻¹⁶ Drastic reduction in lung dose was observed with mDIBH in our study by considering a cutoff value of lung V_{20} (both lungs) for all 11 patients. In this paper, if one considers the individual case, the negative sign shown implies that some patients are getting more minimum dose and maximum dose compared with FB. The aim of this paper is to highlight these figures. The same types of results were already discussed in case of heart, left lung, and spinal cord also. The results were dependent on anatomy. But there is no consistent data for all the patients as discussed above. Furthermore, the treatment with ABC needs decreased amount of MUs necessary to deliver a treatment fraction. The decrease in treatment time helps to minimize the patient motion during treatment.



FIG. 6: Different phases of the breathing cycle. (Courtesy by Varian)

The solution for all these problems like inconsistency and increased dose to the normal structures can be solved by

- performing scan, plan and treatment with optimal patient positioning and optimal phase of mDIBH,
- accurate contouring with margins including intra fractional shifts during ABC,
- considering the variation in patient shape during treatment,
- fusion with MRI, PET-CT scans with the images that were obtained with ABC in the same phase where planning CT was taken, and
- moving critical structures as much away from target as possible in the BEV of the beams with mDIBH or in any phase in gating technique.

Conclusion

Bases on the results of 11 patients presented in this study, we conclude that radiotherapy of lung cancer with ABC has the potential to reduce the mean dose to heart, lung, and spinal cord compared with free breathing in most of the cases. ABC technique needs fewer MUs, thus decreasing the treatment time which further provides patient comfort. ABC technique can immobilize the tumor position but there is no guarantee that it can spare critical structures for all patients compared with FB. This is due to the possibility of critical structures coming into the field for longer time in ABC technique, and patient's anatomy, which influences the results.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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