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Dosimetric Evaluation Of The Impact Of Active Breathing Control (ABC) System On Physical Lung Dose-Volume Parameters In Patients Receiving Consolidative Radiation Therapy (RT) For Extensive Stage Small Cell Lung Cancer (ES-SCLC)

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ABSTRACT

Patients with extensive stage small cell lung cancer (ES-SCLC) suffer from impaired pulmonary functions due to their disease burden and avoidance of radiation therapy (RT) related pulmonary toxicity is of utmost importance. Within this context, efforts have been focused on improving the toxicity profile of radiation delivery by incorporating of contemporary RT techniques. Active Breathing Control (ABC) system has been developed for the management of respiratory motion in thoracoabdominal tumors by achieving reproducible breath holds. In this study, we evaluate the impact of the ABC system on physical lung dose-volume parameters (DVH) in patients receiving consolidative RT for ES-SCLC. For 16 patients referred to our clinic, two different RT plans with and without the ABC system were created and the mean lung dose (MLD) and V20 were analyzed. MLD and V20 were 2267 cGy and 36.7%, respectively at free breathing. MLD and V20 were 1882 cGy and 28.5%, respectively incorporation of the ABC system. The inclusion of the ABC system in consolidative thoracic RT therapy resulted in a 16.98% and 22.34% reduction in MLD and V20, respectively. For the radiotherapeutic management of ES-SCLC, the ABC system is considered to contribute to the treatment.

Keywords: *Extensive stage small cell lung cancer (ES-SCLC), radiation therapy (RT), active breathing control (ABC)*

INTRODUCTION

Lung cancer is a major and global health concern as a leading cause of cancer-related morbidity and mortality around the globe (1,2). Histologically, 2 major types of lung cancer include small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is the most frequent type of lung cancer, however, SCLC is typically associated with a worse prognosis and more limited survival which may be partly attributed to a relatively shorter doubling time and higher growth fraction (3-5). SCLC may be traditionally divided into limited- stage SCLC (LS-SCLC) and extensive-stage SCLC (ES-SCLC) as per the Veterans' Administration Lung Study Group (VALSG) two-stage classification scheme (6,7). LS-SCLC accounts for approximately one-third of all SCLC cases, and typically follows a more favorable disease course compared to ES-SCLC. However, ES-SCLC is defined as a disease extending beyond a single hemithorax which may not be encompassed within a tolerable radiation portal that can include malignant pleural or pericardial effusions, contralateral hilar or supraclavicular lymph nodes, and hematogenous metastases typically leads to a limited lifespan of affected patients (7,8). Unfortunately, ES-SCLC accounts for the majority of SCLC cases and has a grim prognosis. Nevertheless, systemic therapy and radiation therapy (RT) may be used for management of ES-SCLC. Due to the systemic disease burden at the outset, systemic therapies are more frequently utilized for the initial management of ES-SCLC. RT may be reserved for palliation of symptoms, however, there may also be a role for consolidative thoracic RT in selected patients with ES-SCLC (9-11). While the primary advantage of consolidative thoracic RT may be improved progression-free survival of patients with ES-SCLC, optimal dose and fractionation have yet to be a defined (9-11). Given the typically high disease burden within the thorax, radiotherapeutic management of ES-SCLC may pose a formidable challenge to treating physicians. Respecting dose-volume limitations for critical organs has been a pertinent component of optimal thoracic RT to avoid adverse radiation effects. Since patients with ES-SCLC typically suffer from impaired pulmonary functions due to their disease burden, avoidance from RT-related pulmonary toxicity is of utmost importance. Within this context, efforts have been focused on improving the toxicity profile of radiation delivery by incorporating of contemporary RT techniques. Active Breathing Control (ABC) system has been developed for the management of respiratory motion in thoracoabdominal tumors by achieving reproducible breath holds (12-16). In this study, we evaluate the impact of the ABC system on physical lung dose-volume parameters in patients receiving consolidative RT for ES-SCLC.

METHODS

A total of 16 patients referred to our department for consolidative thoracic RT was assessed. Written informed consent of all patients were obtained before consolidative thoracic RT with institutional tumor board approval at our tertiary cancer center, and this study has been conducted in compliance with the Declaration of Helsinki principles and its later amendments. Physical lung dose-volume parameters of V20 and MLD were extracted from the dose volume histograms (DVH) and comparatively analyzed. All patients had previously received systemic therapy for ES-SCLC, and decision-making for consolidative thoracic RT was based on collaborative multidisciplinary evaluation by a group of experts from radiation oncology and relevant thoracic oncology disciplines. Therapeutic strategies were individually considered by taking into account patient, tumor, and treatment characteristics as well as lesion size, localization, and association with surrounding critical structures, symptomatology, and expected outcomes of radiotherapeutic management. Details of the ABC procedure were previously published (16). Briefly, an introductory training session with the ABC device (ABC, Elekta, UK) was performed for each patient to improve compliance and determine individual breath-holding levels. The typical threshold for breath holding was set at 70% to 75% of maximum inspiratory capacity, referred to as moderate-deep inspiration breath holding (mDIBH). Patients were trained on an individual basis to achieve a steady breathing pattern. After practice for breath holding, it was assumed that all patients reached a satisfactory level of mDIBH reproducibly. Following the training session, patients were scanned at free breathing and mDIBH with 3.75 mm slice thickness at Computed Tomography (CT) simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) with arms above head, immobilized by use of a Wing-Board (CIVCO, Kalona, IA, USA). A nose clip was used to ensure breathing through the mouth only, and the mirror enabled patients to see their breathing pattern on the monitor attached to the ABC system which assisted in achieving a steady breathing pattern required for RT simulation and treatment. After acquisition of CT-simulation images, they were transferred to the delineation workstation via the network. Advantage Sim MD simulation and localization software (Advantage SimMD, GE, UK) has been utilized for the delineation of treatment volumes and normal tissues on both free breathing and ABC-mDIBH scans using the same window-level values. For the purpose of this study, lung dose-volume parameters were retrieved from dose-volume histograms and assessed comparatively.

RESULTS

Expert radiation physicists performed radiation treatment planning by taking into consideration the reports of American Association of Physicists in Medicine (AAPM) and the International Commission on Radiation Units and Measurements (ICRU). Two different plans were generated for each patient with and without the incorporation of the ABC system. Beam organizations, wedges, and beam angles were identical in both plans with and without the incorporation of the ABC system. Coverage of the clinical target volume by the 95% isodose line was required, however, planning target volume coverage with the 95% isodose line could not be accomplished for some patients to avoid violation of normal tissue dose constraints. Calculation of treatment dose has been performed by taking into account electron density, CT number, and HU values in CT images with consideration of tissue heterogeneity. Physical lung parameters including V20 and mean lung dose (MLD) were extracted from the dose volume histograms of each patient and analyzed.

Table 1 shows lung dose-volume parameters acquired from treatment plans with and without incorporation of the ABC system.

Table 1. The relationship between mean p53- and Ki67-positive cell numbers

	Dose-volume parameter (mean)	
	V20 (%)	MLD (cGy)
Plan at free breathing without incorporation of the ABC system	36.7%	2267 cGy
Plan with ABC-mDIBH	28.5%	1882 cGy
Percentage reduction by incorporation of the ABC system (%)	22.34%	16.98%

Mean MLD and V20 were 2267 cGy and 36.7%, respectively at free breathing. Mean MLD and V20 were 1882 cGy and 28.5%, respectively with incorporation of the ABC system. In this context, decrease in MLD and V20 was and 16.98% and 22.34%, respectively.

DISCUSSION

Management of respiratory motion is an indispensable component of successful RT administration in thoracoabdominal tumors. ABC system has been introduced as a viable method of respiratory motion management (12-16). ABC system should be used at a certain threshold to ensure reproducible breath-holding. The system uses a digital spirometer and a balloon valve connected to it. In the ABC method, the patient breathes through the mouthpiece in free breathing. Then the system is activated and the balloon valve closes at the defined breath holding phase. The patient is instructed to reach the determined threshold lung volume after a few preparatory free breaths. The valve is inflated with the air compressor for a predetermined time, thus allowing the patient to hold their breath. Breath-holding time usually ranges between 15 to 30 seconds and this breath-holding time typically depends on the individual performance of the patient. After a short rest, the patient should be able to stand for some time so that another consequent breath-holding could be possible. The ABC system may allow for using tighter internal margins to account for respiratory motion which may result in reduced exposure of normal lung tissue. Also, expansion of the lungs at mDIBH may decrease doses to normal lung. Within this context, a critical gain may be acquired by the use of ABC system. Previously, our group reported the utility of ABC guided RT for non small cell lung cancer with detailed dosimetric analysis (16). Effect of ABC-mDIBH on tumor motion and critical organ doses has been assessed in a series of 23 patients with locally advanced NSCLC. Individual tumor motion of patients with and without ABC-mDIBH was documented and comparatively analyzed. As the outcome, the incorporation of ABC-mDIBH in NSCLC management resulted in improvement in physical lung parameters of V20 and MLD which are predictors of radiation pneumonitis. It was concluded that ABC-mDIBH increased normal lung tissue sparing in definitive NSCLC RT through improving physical lung parameters by excellent tumor immobilization. The authors reported that the incorporation of ABC-mDIBH into NSCLC RT could offer implications for potential margin reduction and dose escalation to improve treatment outcomes further (16).

In conclusion, respiratory movement of tumors and organs in the thoracic region may lead to inaccuracies in target definition, treatment planning and delivery, along with discordance between planned and delivered dose distributions. Difficulties in the precise characterization of individual tumors and organ motility may pose a major obstacle to the administration of RT. This situation may become even more critical in the setting of hypofractionated regimens or Stereotactic Body Radiotherapy, where high-fraction doses are delivered in a limited number of fractions. For this reason, it is a necessity to deal with breathing-induced movement for radiotherapeutic management of lung cancer. While the definition of small internal margins without respiratory motion management may cause geographic miss and resultant treatment failures, definition of large internal margins to account for respiratory motion may increase treatment morbidity and preclude delivery of curative intent RT due to violation of critical organ dose constraints.

ABC system offers a viable method of respiratory motion management for lung cancer RT as addressed in several studies (12-16). Reduction in critical organ doses by elimination or minimization of internal margins by use of the ABC system may allow for dose-escalated RT which may improve tumor control probability and treatment outcomes. Further studies are needed to assess the utility of the ABC system for radiotherapeutic management of ES-SCLC.

Conflict of Interest

There are no conflicts of interest and no acknowledgements.

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