International Journal of Computational and Experimental Science and Engineering (IJCESEN)
Vol. 5-No.3 (2019) pp. 142-146
http://dergipark.org.tr/ijcesen

ISSN: 2149-9144

Research Article

Investigation of The Effect of Intermediate Dose Calculation Module on Dose Distribution in Lung Cancer Radiotherapy Patients

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Article Info:

DOI: 10.22399/ijcesen.626510
Received : 30 September 2019
Accepted : 31 October 2019

Keywords

Lung Cancer
IMRT
Intermediate Dose Calculation
Optimization

Abstract:

The aim of this study was to investigate the effect of the use of intermediate dose calculation module on dose volume histogram (DVH) during dose optimization in the treatment plans of radiotherapy patients diagnosed with lung cancer. This study was carried out by using Eclipse (Version 15.3) treatment planning system with Trilogy model Linear Accelerator device in Radiation Oncology Department of Şişli Hamidiye Etfal Training and Research Hospital. Ten patients with lung cancer were included in the study. In this study, critical organ doses, conformity index (CI) and homogenity index (HI) were compared by making optimization in cases where intermediate dose calculation module was active and inactive. The plans using the Intermediate dose calculation model are more homogeneous and uniform. Differences between critical organ doses, conformity index (CI) and homogenity index (HI) were statistically significant when using the intermediate dose calculation module. It has been demonstrated that the intermediate dose calculation method in heterogeneous lung cancer patients is superior in terms of dose homogeneity and tumor volume enveloping, which improves the quality of treatment plans.

1. Introduction

While lung cancer is a rare disease in the early 20th century, its frequency has gradually increased in parallel with the increase in smoking habits and has become the most common type of cancer in the world [1]. Lung cancer is responsible for 12.8% of cancer cases and 17.8% of cancer deaths worldwide [2]. Lung cancer, which constitutes one third of all cancer deaths in our country, is the most common type of cancer in men. It is incidence and mortality are parallel to the prevalence of smoking. Although the incidence rate increases after the 70s, the rate of lung cancer in men is higher than in women. On the other hand, the incidence of males decreased in recent years and increased in females. Squamous cell carcinoma is the most common histological type. Adeno cancer is more common in women and non-smokers [3]. When the passive cancer data of the Ministry of Health in our country are examined, it is seen that the incidence of lung cancer in our western regions is higher than our eastern regions [4]. Trachea, bronchial and lung cancer (YSH in 52.5 / 100000 people) and breast cancer in women (YSH in 43.0 / 100000 people) are the most common types of cancer in 2017 research conducted by the Ministry of Health. When the stages of lung cancer are examined, it is seen that 52.7% make distant metastasis. Diagnosis of lung cancer is usually late. In our country, the decreasing trend seen in both lung cancer and tobacco-related cancers, especially in men, continues. However, this decline may turn into an increase in cancer statistics in the coming years with the increasing tobacco use in recent years [5]. When deciding on the treatment of lung cancer, treatment is planned considering the general and

performance status, age, concomitant diseases, heart and lung functions. The treatment approach for small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) is different. Surgery is considered the most effective method in the treatment of early stage NSCLC. Adjuvant radiotherapy has been reported to reduce local recurrences. Adjuvant radiotherapy is recommended in the presence of mediastinal lymph node metastasis or close / positive surgical margin after surgery. Adjuvant chemotherapy is recommended in patients with stage IB-III. In locally advanced patients, surgery may be performed simultaneously after chemoradiotherapy (CRT) or neoadjuvant therapy. The role of surgery in SCLC is uncertain. Chemotherapy is the standard treatment for advanced disease. Concurrent CRT is recommended in limited stage disease in the early period. CRT may be administered simultaneously in advanced stage cases responding to chemotherapy. Prophylactic cranial radiotherapy is recommended in patients with SCC who are unlikely to receive chemotherapy for brain metastases. Palliative radiotherapy may be used to treat metastasis and tumor related symptoms [6]. The aim of radiotherapy is to maintain homogenous radiation dose distribution in the target volume and to maintain maximum protection of intact tissues. Conventional radiotherapy provides this purpose, while the normal tissues can be irradiated with a larger tumor [7]. The main goal in radiotherapy is to keep the normal tissue dose to a minimum and to give the appropriate homogenous dose to the target volume. This is not possible with conventional techniques that are common today. In recent years, the most suitable (conformal) dose distribution in the target can be achieved with the intensity modulated radiation therapy (IMRT). This treatment technique allows for better protection of healthy tissues, allowing higher doses to be achieved in the tumor, thereby providing improved tumor cure. The use of IMRT has been very useful in terms of optimization of radiotherapy (dose increase for target volume, reduction of risk organ dose, and dose homogeneity). IMRT is an advanced form of three-dimensional conformal radiotherapy (3DCRT) treatment. In IMRT, conformal dose distribution is achieved with the help of the multi-leaf collimator (MLC) in the head of the linear accelerator. Unlike conventional or conventional conformal therapy, the dose intensity of each IMRT area is varied in a complex way. IMRT is like an upper step in conformal radiotherapy. However, it allows non-uniform dose distribution. An acceptable dose distribution of the target volume is achieved by preserving healthy tissues [8]. Dose intensities are achieved using different optimization techniques. Dose intensities are calculated according to the thickness of the tumor tissue and healthy tissue regions with segments formed by MLC. This ensures an acceptable homogeneous dose and maximum protection in healthy tissues close to the tumor. The radiation oncologist should be informed in advance which dose is sufficient for the tumor and which dose is the limit for the critical organ. Many treatment planning computers require the user to enter energy, beam size, angle and amount. Then it performs an iterative calculation with this information. IMRT is implemented in two ways:

The first is the dynamic IMRT (DMLC) technique created by continuous movement of collimator leaves during irradiation, and the second is the step and shoot technique (SMLC), where rays are divided into lower segments [9, 10]. IMRT plans are more suitable for concave organs. IMRT includes complex dose calculations. Therapy planning computers need more computing time. At this point, more powerful algorithms are needed. Multiple treatment sites and multiple sub-segments take a long time to calculate. The Varian Treatment Planning System (TPS) Eclipse v11 Analytical Anisotropic Algorithm includes an option to perform intermediate dose calculation during optimization using Analytical Anisotropic Algorithm (AAA). The new plans were created using this intermediate dose calculation during optimization with the same planning objectives and dose restrictions as the original plan. The balance between efficiency and accuracy of simplified and accurate dose calculation algorithms is expressed by differences between optimized and final dose distribution taking into account tissue heterogeneity. This can be observed in the lung, particularly under small field geometries of the lateral electronic balance between tissues of different density [11, 12, 13]. Previous studies have investigated changes in the final dose distribution of IMRT plans using fast dose calculation algorithms during the IMRT optimization process [13, 14, 15]. However, minimal information is available to understand the potential impact of the intermediate use of less accurate dose calculation algorithms on the quality and effectiveness of the optimization results and on the final plan quality. This effect may be more pronounced when planning IMRT for lung cancers where the difference in electron density between air and water is important. A new feature added to Eclipse v11 allows the calculation of an intermediate dose distribution during optimization using AAA. The aim of this study was to compare the dosimetric parameters and optimization efficiency of the planned target volume (PTV) and organ at risk (OAR) for the active and inactive IMRT plans of 10 randomly selected lung radiotherapy patients diagnosed with lung cancer.

2. Material Method

Ten randomly selected patients with lung cancer who were admitted to Şişli Hamidiye Etfal Training and Research Hospital were included in the study. Computed tomography (CT) images were obtained by holding the supine, arms over the head, T-bar / wingboard and tilting the knees to the gantry side. CT extraction is performed by placing CT marker markers at the intersection of isocenter midline and side lasers on the patient. The image of the region between the upper boundary of the L2 vertebra and the cricoid cartilage, covering all lungs, is taken at a cross-sectional thickness of 3 mm. Inpatient positions of patients during CT scan are maintained in the same way throughout their treatment. CT section images are transferred to the treatment planning system via Digital Imaging and Communication in Medicine (DICOM). Before the treatment, CT, Positron Emission Tomography-Computed Tomography (PET-CT) and Magnetic Resonance Imaging (MRG) are obtained by transferring CT sections to contouring computers and treatment volumes are drawn and dose definition is made. It is recommended to give 50-66 Gy in adjuvants according to surgical margins and 60-74 Gy in definitive treatments in NSCLC. Although optimal radiotherapy has not been fully established in SCLC, 50-70 Gy is recommended in conventional fractions and 45 Gy in hyperfraction is recommended [6]. For the treatment plans prepared with the IMRT technique, the dose prescription was given to the patients in 30 fractions and 200 cGy per fraction as a total treatment dose of 6000 cGy. The dose rate was selected as 600 MU. Plans of the treated patients were made using Varian Eclipse (Version: 15.3) Treatment Planning System (TPS) using AAA and AAA Intermediate dose optimization algorithms. 95% of PTV was normalized to receive the full dose. The optimization page of the treatment planning computer includes the dose values we want the PTV to include and the permissible dose limits for the critical organs; Spinal cord ≤50 Gy; Lung V20 ≤ 35, V5 ≤ 65, MLD ≤ 20 Gy; Heart V40 ≤ 80%, V45 ≤ 60%, V60 ≤ 30%, Mean ≤ 35 Gy; Esophagus Mean ≤ 34 Gy, Max 105% of prescription dose; Tolerance dose values have been defined to provide max. 66 Gy of brachial plexus. During optimization, priority values indicating the order of priority to be given while trying to provide the specified dose values for PTV and critical organs were entered on the optimization page. MINITAB program was used for the dose optimization algorithms where the dose values, conformity index (CI), homogeneity index (HI) values of target volume and critical organs were read from the dose-volume histograms of the treatment plans, and t-test was used for the statistical data. IMRT areas and dose distribution are shown in figüre 1.

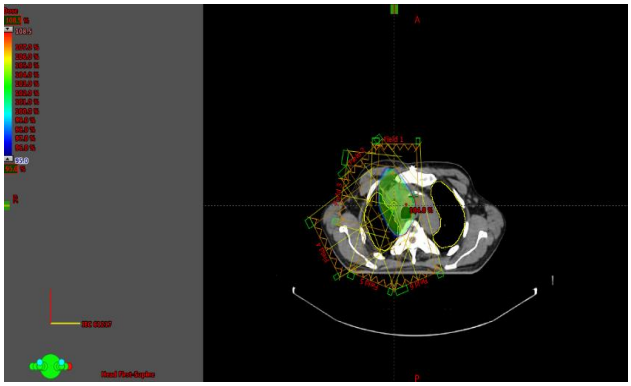

Figure 1. *Display of IMRT fields and dose distribution.*

3. Results

The plans using the Intermediate dose calculation module are more homogeneous and uniform. When the Intermediate dose calculation module is used, the differences between critical organ, CI and HI values are statistically significant. The ideal value for the CI value is 1. Although this is often not possible, a plan that provides close to 1 value is accepted. This value was calculated according to equation 1.1 [10].

When CI> 1, the irradiated volume means that it is greater than the target volume. In the case of CI <1, the target volume is partially irradiated [16].

$$CI = VHV \times VTIH / (PTVPIH)^2 \quad (1.1)$$

From the terms in Equation 1.1, VHV refers to PTV volume, VTIH refers to the defined 95% isodose volume, and PTVPIH refers to the PTV volume wrapped by the 95% isodose line.
The homogeneity index value indicates the homogeneity of the dose distribution in PTV. The closer this value is to 0, the more homogeneous the dose distribution is called. Homogeneity index values of the plans were calculated according to equation 1.2 [17].

$$HI = (D\%2 – D\%98) / D\%50 \quad (1.2)$$

In terms of Equation 1.2, D2% refers to the dose received by 2% of the target volume, D 98% refers to the dose received by 98% of the target volume, and D 50% refers to the dose received by 50% of the target volume. In accordance with the data obtained from the dose-volume histograms obtained from the optimization of treatment plans, the dose-volume values of the critical organs and the CI and HI parameters of the target volumes are compared and given in Table 1.

Table 1. *Mean and standard deviation values of critical organs and CI, HI doses for two different optimizations*

	Mean ± Standard Deviation (cGy)		
	AAA Algorithm Intermediate Dose Used	AAA Algorithm Intermediate Dose Unused	P Value
Heart	975,53 ± 612,33	1005,5 ± 615,72	0,0072
Medulla Max.	3753,5 ± 936,35	3823,3 ± 942,56	0,001
CI	1,2766 ± 0,0863	1,3222 ± 0,1222	0,000
HI	0,1302 ± 0,0275	0,1662 ± 0,0200	0,001
Esophagus	1897,6 ± 1009,64	1936,3 ± 1022,03	0,001
Lung-PTV	18,21 ± 6,54	18,32 ± 5,58	0,184

Data MINITAB program was used for 10 patient data and t- test was used for matched data. Alpha (α) value was accepted as 0.05 and the test was performed at 95% confidence level. ($p < 0.05$ was considered significant). Since $P > \alpha$, h0 red, h1 hypothesis was accepted. Since $P < \alpha$ is alpha, h0 is accepted, h1 hypothesis rejected.
Established hypothesis:
h0: AAA Algorithm Intermediate Dose Used = AAA Algorithm Intermediate Dose Not Used
h1: AAA Algorithm Intermediate Dose Used> AAA Algorithm Intermediate Dose Not Used

4. Conclusions

The choice of dose calculation algorithm and how it is incorporated into the IMRT optimization affects the speed, accuracy and optimality of the final dose distribution. Further dose calculation algorithms, such as AAA, use multiple photon nuclei derived from Monte Carlo modeling to account for complex tissue heterogeneity in the patient body. In many treatment planning systems, a rapid dose calculation algorithm is normally used to provide repeated dose calculations during optimization to ensure that optimization is completed quickly. Approaches and simplifications used by these rapid dose calculation algorithms to achieve dose calculation speed may result in final dose errors. It is useful to perform an intermediate dose calculation using AAA during optimization, in particular in the case of deviation from the Dose Volume Histogram (DVH) generated from the final dose calculation, the DVH calculated during the optimization process [13].This usually occurs when there are density heterogeneities in the volume being treated. This is in contrast to the original optimization process, where transient approaches, such as the use of optimization structures, are used to compensate for cold spots within the PTV, and manual adjustment of parameters during re-optimization is often performed for reduction purposes. The results of this study showed that the use of an intermediate dose module during the optimization process both improved lung IMRT plan quality and planning efficiency. In terms of the acceptability of the lung treatment plans, the doses to which the critical organs were exposed were ensured to not exceed the permissible dose limits specified by the NCCN. The CI and HI values defined for the target volumes were calculated in accordance with International Radiation Units and Measurements Commission (ICRU) protocols. In lung cancer patients representing heterogeneous environment, it has been demonstrated that the module of intermediata dose calculation method improves the quality of treatment plans and is superior in terms of dose homogeneity and coverage of tumor volume. Critical organ doses, CI and HI values of lung plans prepared using Intermediate dose calculation module were found to be better than other systems. The Intermediate dose calculation module has been shown to improve the quality of treatment plans in areas with low-density organs such as the lung. Vanetti et al. reported that the plan quality of the plans made with the intermediate dose calculation module increased, the risky organs were better protected, the homogeneity of the dose distribution increased [18]. The results obtained in this study were similar to those in the literature and it was found that the organ at risk doses were lower and the homogeneity index and conformity index were better than the planning results obtained from other systems. Monica et al. in their study, the treatment plan for 10 patients with lung cancer using AAA and AAA intermediate dose modules found the mean and standard deviation values of HI 0.17 ± 0.02 and 0.11 ± 0.01 respectively [19]. In our study, HI values were found to be better when AAA intermediate dose module was used. Treatment plans with and without intermediate dose calculation were compared in terms of targeting and OAR dosimetry and planning effectiveness. The results showed that for IMRT treatment planning of lung cancer, the use of intermediate dose calculation during optimization significantly reduced treatment

planning time, while improving dose homogeneity and reducing the maximum dose to PTV. OAR dose reduction was small, but still statistically significant. In statistical analysis; Heart, Medulla Max, Esophagus, Pulmonary CI and HI values for ten (10) patients, the mean ± standard deviation (cGy) doses, using the AAA algorithm intermediate dose method, the critical organ doses were superior to the AAA algorithm intermediate dose plan the difference has been confirmed.

Acknowledgement

The study was a retrospective study and the ethics committee decision was taken as 2443.

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