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Is It Time to Reconsider the Need for the ITV In SBRT For Lung Tumors?

Viacheslav Soyfer[1*], Benjamin W. Corn M.D[1], Nir Honig B.S[1]

[1]*University of Tel Aviv/Tel Aviv Sourasky Medical Center, Israel*

**Corresponding author: Dr. Viacheslav Soyfer, University of Tel Aviv/Tel Aviv Sourasky Medical Center, Israel, Tel: 972524266553; Email: slavas2506@gmail.com*

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Abstract

Purpose: The importance of tumor positioning for SBRT is self-evident. There has been marked evolution in the last decades from 2D through 3D and IMRT to the utility of IGRT and four dimensional tumor localization that has enabled prescription of high doses of radiation to small tumor volumes. 4D simulation reduces the likelihood of "geographic miss". We developed a model involving fusion of images from 4D followed by free breathing CT.

Methods and Materials: We analyzed 13 treatment planning datasets from our initial cohort of patients who underwent SBRT for primary lung cancer or oligometastases to the lung. We carried out 4-D simulation and constructed the ITV. We sought to determine whether the respective centers of the ITV and GTV are concordant. Comparison is predicated upon the fusion of the 3-D and 4-D CT simulation datasets. The deviation of the location of the isocenters of the ITV and the captured GTV was registered individually.

Results:

The mean distance from the isocenters of the GTV and ITV was 4.28 mm (SD 2.06.) in CC, 0.75 (SD 0.57) in LM and 1.08 (SD 0.95) in AP directions.The isocenters of the ITV were found in the central positions (from 4 to 5 segments) in 2 cases (15%). The tumor position in the peripheral segments (1 to 3 and 6 to 8) was found in 11 cases (85%)In 6 cases (46%) the range of motion was extremely high (segments 1 to 2 and 7 to 8)

Conclusions: The center of the static GTV consistently deviates from the ITV center. It is mandatory to implement the ITV-based technique to be certain that in a non-forgiving, high-dose approach (i.e., SBRT) the appropriate targets are indeed encompassed.

Keywords: SBRT; 4D Simulation; ITV; Lung

Introduction

Stereotactic Body Radiation Therapy (SBRT) is becoming a standard treatment for early stage lung cancer and oligometastases from other primary malignancies. The basic principle of SBRT is the delivery of high dose radiation therapy to relatively small volumes of tissue with maximal sparing of normal structures. A major obstacle encountered in the delivery of SBRT for lung tumors is the unpredictability of respiratory motion of each patient. There has been marked evolution in the last decades from 2D through 3D and IMRT to the utility of IGRT and four dimensional tumor localization that has allowed prescription of high doses of radiation to small tumor volumes [1]. There are many studies that have tried to decipher the physiologically-based range of motion of the pulmonary structures as a function of their location [2-7]. It has been established that there is greater movement in the lower lobes when compared to middle and upper lobe motion [8].

No uniform agreement exists among radiation oncologists; however, regarding the threshold tumor size that justifies the use of respiratory management techniques. The American Association of Physicists in Medicine (AAPM) Task Group 76 recommends that tumor motion management should be applied when the range exceeds 5 mm in any direction [9]. The significance of such a recommendation in tumors of varying size and the relative benefit of sparing normal lung tissue are less well described. In practice many institutions use standard CT simulation without attempting to learn the habits of individual patients vis-a-vis respiratory motion in cases of small (less than one centimeter) tumors, especially in the upper and middle lobes. Determination that there is benefit to 4-D CT simulation is usually a matter of clinical judgment. Embedded within the decision-making process is the understanding that 4-D CT simulation behooves significant increases in radiation exposure to the patient. Another factor pertains to the recognition that the lungs of patients suffering from COPD have limited expansive capability, therefore, relegating 4-D technologies to marginal benefit. Further, tumors located in the upper lobes of the lungs are characterized by insignificant motion [2]. These negative considerations are underscored by the reality that 4-D technologies usually entail irradiation of greater pulmonary volumes. Notwithstanding, it is clear that with static CT one is never sure where the tumor was encompassed and even, when encompassed there is uncertainty that the PTV margin is sufficient to cover the total motion of the tumor.

In our institution, we studied the potential clinical error of the location of the isocenter of the Gross Tumor Volume (GTV) found on the standard "static" simulation versus the isocenter of the Internal Target Volume (ITV) generated by 4D imaging and interposed (fused) based on the bony landmarks (mostly vertebrae). We attempted to determine whether the respective centers of the ITV and the GTV are concordant. Comparison is predicated upon the fusion of the 3-D and 4-D CT simulation datasets.

Methods

We retrospectively analyzed 13 treatment planning datasets on the initial cohort of lung cancer patients and patients with oligometastases from other primary malignancies who underwent SBRT at our institution. Traditionally, we like most centers, performed static CT simulation (Phillips Brilliance Big Bore) with the addition of sufficient margins to account for motion. During the past year, we have carried out 4-D (eight-phase) simulation and constructed an internal target volume (ITV).

Patients were usually situated in the supine position with arms above the head. Immobilization was achieved using a vacuum bag. The pre-simulation imaging (CT, PET CT) was used to determine the swath of the scan for 4D purposes in the smallest possible range to include the potential tumor motion. The analysis of the tumor movement was performed thereafter. All patients then underwent standard CT simulation when the decision was made to create the ITV. Patients who were managed by breath control techniques were not included in the study and subsequently underwent separate simulation. Each ITV dataset was divided throughout the entire track along the cranio-caudal (CC), lateral- medial (LM) and anterior-posterior (AP) directions into eight arbitrary segments to form an 8 x 8 x 8 matrix (Figure 1). The deviation of the location of the isocenters of the ITV and the captured GTV was registered individually in the cranio-caudal, anterior-posterior and lateral- medial directions. In the CC axis, the most inferior position was numbered as "one" and the most superior as "eight." The central position was designated as being in segments four through five.

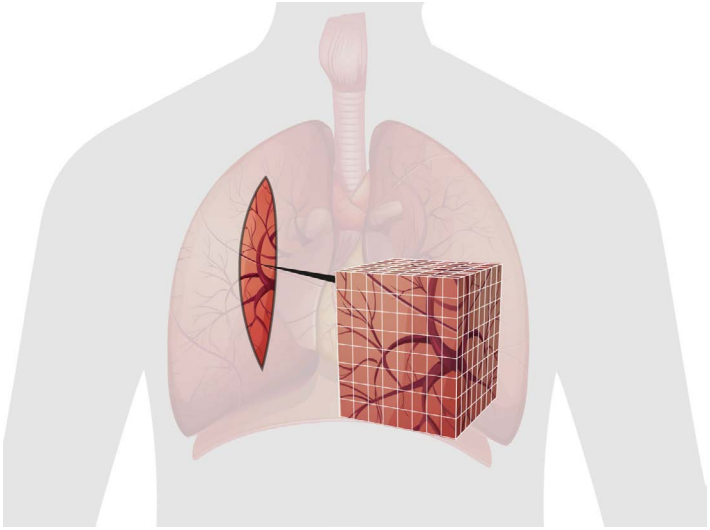


Figure 1. The illustration depicts the division of the tumor tract in eight segments.

The mean values and standard deviation for the entire group were calculated.

Results

Thirteen patients were analyzed in the study. There were 6 men and 7 women. Seven patients were treated for primary carcinoma of the lung and 6 were irradiated for metastases to the lung. The mean age of the patient groups was 63 (table 1).

Table 1. Patient characteristics.

number	gender	age	diagnosis
1	f	67	lung
2	m	79	lung
3	m	78	lung
4	m	67	colon
5	f	87	sarcoma
6	m	65	lung
7	f	21	sarcoma
8	f	43	sarcoma
9	m	64	sarcoma
10	f	58	sarcoma
11	m	55	kidney
12	f	62	colon
13	m	74	lung

f- Females; m- Males;

The mean volume of the GTV was 0.68 cc (SD: 0.37). The mean volume of the ITV was 3.14 cc (SD: 1.63). In one case, the tumor volume differed significantly from the mean value (GTV-30.1 cc and ITV 60.4 cc).

The mean distance from the isocenters of the GTV and ITV was 4.28 mm (SD: 2.06.) in the cranio-caudal axis, 0.75 mm (SD: 057) in the Lateral-Medial dimension and 1.08 mm (SD: 0.95) in the AP direction (Table2).

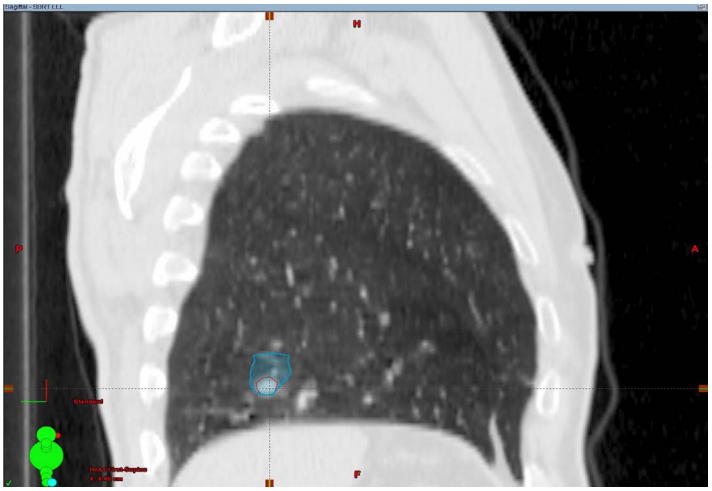
The isocenters of the ITV were found in the central positions (from 4 to 5 segments) in 2 cases (15%). The tumor position in the peripheral segments (one to three, and, six to eight) was found in 11 cases (85%) Fig 2.

In 6 cases (46%) the range of motion was extremely high (segments 1 to 2 and 7 to 8) (table3).

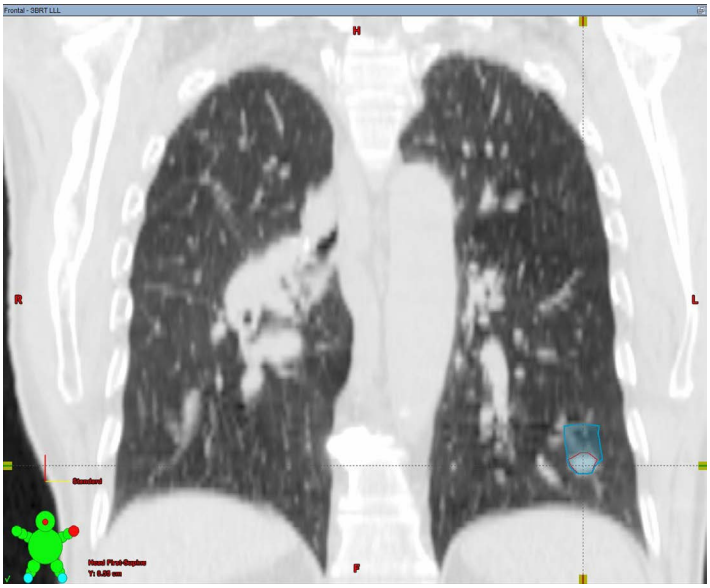
Table 2. Absolute distance between the GTV and ITV centers for the patients studied.

CC (mm)	AP (mm)	LM (mm)
5.3	2.5	1.9
5.6	1.3	1.1
3.9	3.3	0.1
2.1	0.6	1.4
0.8	1.7	0.7
2.4	0.8	1.4
6.4	0.4	0.5
6.2	1.3	0.6
2.5	0.2	0.5
4.8	0.3	0.1
4	0.2	0.2
3.5	0.4	1
8.2	1.1	0.2

LM- lateral- medial; AP- anterior-posterior; CC- cranial- caudal



a. Lateral view



b. Coronal View

Figure 2. Depicts the example of the most peripheral tumor location captured on standard simulation vis-a-vis the tumor motion track.

Table 3. The frequency of GTV's center appearance related to ITV's centers.

CC	APPA	LM
2	4/5	4/5
2	4/5	4/5
5	4/5	4/5
3	4/5	4/5
4	4/5	4/5
6	4/5	4/5
7	4/5	4/5
7	4/5	4/5
6	4/5	4/5
2	4/5	4/5
3	4/5	4/5
6	4/5	4/5
1	4/5	4/5

LM- lateral- medial; AP- anterior-posterior; CC- cranial- caudal

Discussion

SBRT is becoming increasingly popular for early stage lung cancer and oligometastases. Precise tumor positioning for SBRT is facilitated with 4-D planning. The concept of 4-D planning has been well-described in the literature. It is generally accepted that 4-D simulation reduces the likelihood of geographic miss in tumor location.

The definitions of target volumes that must be covered by radiation therapy, described by ICRU Report 62, constitute an infrastructure for the planning and delivery of radiation therapy [10]. For lung cancer, it is accepted that the Clinical Target Volume should be expanded 6 to 9 mm around the Gross Tumor Volume depending on the pathology [11]. In the absence of tracking of tumor motion in movable organs, such as lung, the addition of 1 cm contouring in all directions is mandatory to create the CTV [12]. ICRU Report 62 defines the volume formed by the CTV and the internal margin as the internal target volume (ITV). The ITV represents the movements of the CTV as referenced to the patient coordinate system and is specified in relation to iternal and external reference points, which ideally should be rigidly related to each other through bony structures [13].

The movements of the tumor within the lung are unpredictable and depend on several factors, such as the location (upper versus lower lobe), the proximity to the heart, lung elasticity (it's postulated that patients with severe chronic obstructive pulmonary disease (COPD) have lesser lung expansion and correspondingly less tumor movement). The lack of uniformity of tumor location within the established ITV is well described by Nishubishi et al [14].

The creation of the ITV and subsequent PTV often results in significantly larger volumes of radiation as opposed to standard simulation. Wolthaus at al described the creation of the 3D CTV from the time average tumor position [15]. Those who have failed to adopt 4-D technologies rely on the above-mentioned shortcomings including limited expansive capabilities in COPD, insignificant tumor motion in the upper lung lobes, etc. We are skeptical that there is underdosing of irradiation in the most peripheral position of the tumor tract.

We endeavored to decipher the pattern of location of the isocenter of the created volume of the ITV against the center of the GTV depicted on the standard CT simulation. The surprising results of our study show that the captured position on standard simulation is likely to be severely discordant from the isocenter of the ITV in peripheral segments in approximately 50 % of cases. The recommended creation of the CTV and PTV in these cases will therefore geographically miss the target. Technologies for precise tumor positioning and real time delivery planning are rapidly developing. The radiation oncology institutions with access to CyberKnife ™ machines

advocate their use in SBRT due to accuracy in tumor tracking positioning in range of less than one millimeter [16]. Four dimensional delivery systems that integrate the internal position monitoring and accurate real-time beam adaptation are being intensively investigated and most probably provide geometrically ideal dose delivery to moving tumors [17]. Until this is a common clinical practice, the attempts to omit the creation of the ITV should be carefully evaluated. Therefore, the entire motion tract presumably should be addressed for the planning of the PTV, unless the delivery tracking is applied.

Conclusion

Tumor motion management, other than with tracking systems or breath hold techniques, must include the creation of an ITV even for small lung tumors. The standard form simulation harbors the danger of undertreatment of the tumor and overexposure of the normal tissue. The uniqueness of our study is the discovery of the very high frequency of the extremely peripheral position of the tumor in the ITV track.

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