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Medical Physics Contribution:

## A modified formula for dose calculations of stereotactic ablative body radiotherapy for non-small cell lung cancer

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#### ABSTRACT

To provide a modified formula consistent with the Monte Carlo (MC) algorithm for dose calculations during stereotactic ablative body radiotherapy for non-small cell lung cancer. Seventy CyberKnife treatment plans were calculated and analyzed by MC and ray-tracing (RT) algorithms, separately. Parameters of treatment plans were compared, and those associated with differences of dose distributions were analyzed to establish a modified formula. Gross tumor volume and tumor tracking volume (TTV) were defined as the evident disease on the sequences of the window width and level of the lung and the mediastinum. Additionally, the formula was validated by another 20 plans. The prescription dose of the 90 patients was 60 Gy/5f. The RT algorithm overestimated the planning target volume (PTV)  $D_{95}$  by an average of 8.59 Gy and the gross tumor volume  $D_{99}$  by an average of 5.84 Gy. The homogeneity index of PTV was underestimated by 0.11 on average, whereas the conformity index and new conformity index was underestimated by 0.05. The RT algorithm overestimated the dose distribution to the spinal cord by 2.23 Gy, the esophagus by 1.96 Gy, the trachea by 1.89 Gy, the left-sided bronchus by 1.77 Gy, the right-sided bronchus by 1.64 Gy, and the heart by 2.16 Gy. The average whole-lung dose volumes of lung tissues and dose volumes of  $V_5$  were overestimated by 2.69 Gy and 7.52%, respectively. A power function distribution ( $R^2 = 0.8626$ ) was confirmed between PTV D<sub>95</sub> and TTV volumes. PTV D<sub>95</sub> calculated by the MC algorithm could be computed easily with TTV and PTV D<sub>95</sub> calculated by the RT algorithm based on the formula. The modified equation was more consistent with MC algorithm than with other formula, which could be a reference to those not accessible to the MC algorithm.

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#### Introduction

Lung cancer is the leading cause of cancer deaths worldwide.<sup>1</sup> For patients with non-small cell lung cancer (NSCLC), surgery is the preferred treatment. However, for inoperable patients, such as those with other diseases or intolerable to surgeries, radiation therapy is the only alternative curative treatment.<sup>2</sup> More than 95% of patients with early-stage NSCLC treated with stereotactic ablative body radiotherapy (SABR) achieved good local control, with a median survival time of 34 to 45 months. SABR has already become the standard treatment option for medically inoperable patients with early-stage NSCLC.<sup>3-5</sup> The CyberKnife system (Xsight Lung Tracking System) can track tumors located in the lungs when their diameters in all planes are greater than 15 mm. Tumor movement during inhalations and exhalations is traced in real time during the treatment, and simultaneously the treatment beams can be modified automatically, rendering SABR noninvasive for lung cancer with sub-millimeter accuracy. Real-time tracking further reduces the collateral irradiation doses to normal lung tissues and the probability of developing radiation-induced pneumonitis.<sup>6</sup>

The CyberKnife treatment planning system is equipped with ray-tracing (RT) and Monte Carlo (MC) algorithms.<sup>7,8</sup> The dose distributions in non-homogeneous media could be modified by the MC algorithm, which is the most accurate method for calculating dose distributions.<sup>9-11</sup> The RT algorithm, meanwhile, overestimated the planning target volume (PTV) doses by an average of ~19% to 21%.<sup>8,12-14</sup> Up to May 2016, in mainland China, a total of 21 hospitals have introduced CyberKnife. Among them, the third generation of CyberKnife (G3) was not equipped with the MC algorithm. In addition, only part of the fourth (G4) and fifth generation (VSI) CyberKnife provided the MC algorithm. Therefore, the aim of our study was to establish a modified formula for dose calculation.

#### **Methods and Materials**

#### Patient selection

Seventy patients with NSCLC who had received CyberKnife between June 2013 and June 2015 were retrospectively analyzed. Patients who met the following criteria were included: a diagnosis of NSCLC confirmed by biopsy specimen; aged 18 to 80 years; with an inoperable condition or refusing surgeries; with 1 peripheral lesion, the diameter of which was between 1.5 cm and 8 cm (8 cm was included); with an expected survival of more than 6 months; with an Eastern Cooperative Oncology Group scale no more than 2; no previous radiotherapy; no multiple lesions; and no distant metastases. Forty-two male and 28 female patients were included in the study, with a median age of 64 years. The study set consisted of 3 cases of large cell lung cancer, 27 cases of squamous cell carcinoma, and 40 cases of adenocarcinoma. Of the 70 foci, 11 were located within the right upper lobe, 15 within the right middle lobe, 7 within the right lower lobe, 25 within the left upper lobe, and 12 within the left lower lobe. The average diameter of tumors was 3.40 cm, and the median was 3.21 cm.

#### Definition of variables

Gross tumor volume (GTV) was delineated as a radiographically evident gross disease acquired from the image sequences of the window width and level of the lung. PTV was the expansion of 5 mm outside the GTV. Tumor tracking volume (TTV) was defined as the contour of the tumor on the sequences of the window width and level of the mediastinum (Fig. 1). PTV  $D_{95}$  and GTV  $D_{99}$  were defined as the dose to 95% volumes of PTV and 99% volumes of GTV, respectively. The conformity index (CI) was calculated with the equation:  $CI = \frac{V_{iso}}{V_{overlap}}$  (V<sub>iso</sub>: volumes covered by isodose line; Voverlap: overlap volumes of Viso and PTV). The new conformity index (nCl) was calculated with the following formula:  $nCI = \frac{CI}{Coverage}$ . The homogeneity index (HI) was determined by the equation:  $HI = \frac{D_{max}}{R_{xDose}}$  (R<sub>xDose</sub>: prescription dose). The definition of whole-lung  $V_5$  was the percentage of the irradiated lung volume receiving a radiation dose exceeding 5 Gy. Esophagus  $D_{5cc}$ , trachea  $D_{4cc}$ , bronchia  $D_{0.5cc}$ , heart  $D_{15cc}$ , and spinal cord  $D_{0.35cc}$  were the doses to 5 cc of the esophagus, 4 cc of the trachea, 0.5 cc of the bronchia, 15 cc of the heart, and 0.35 cc of the spinal cord, respectively.

#### Treatment planning

The patients adopted a supine position, and were scanned with a large-aperture computed tomography (CT) simulator (Brilliance CT Big Bore Oncology; Philips Medical System, The Netherlands) during inhalation. Scanning conditions were as follows: 120 kVp, 400 mAs, 1.5 mm slice thickness without image intervals (helical), and a 0.938 pitch. The scanning range was set from 15 cm outside of the lower boundary of the tumor to 15 cm outside of the upper boundary of the tumor, including the whole lung. After the CT simulation images with and without contrast were imported into the CyberKnife Data Management System, the GTV and organs at risk (OARs) were delineated. The OARs included the left and right lungs, esophagus, trachea, left-sided and rightsided bronchi, pericardium, and spinal cord. Afterward, the spine tracking volume (STV) (Fig. 2) and TTV were contoured. STV and TTV were used for primary image-guided setup and tracing positions of the tumor during treatment

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