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Original article

Monte Carlo calculations support organ sparing in Deep-Inspiration Breath-Hold intensity-modulated radiotherapy for locally advanced lung cancer

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ABSTRACT

Background and purpose: Studies indicate that Deep-Inspiration Breath-Hold (DIBH) is advantageous over Free-Breathing (FB) for locally advanced lung cancer radiotherapy. However, these studies were based on simplified dose calculation algorithms, potentially critical due to the heterogeneous nature of the lung region. Using detailed Monte-Carlo (MC) calculations, a comparative study of DIBH vs. FB was therefore designed.

Material and methods: Eighteen locally advanced lung cancer patients underwent FB and DIBH CT imaging and treatment planning with the Anisotropic-Analytical-Algorithm (AAA) for intensity-modulated-radio therapy or volumetric-modulated-arc-therapy using 66 Gy in 33 fractions. All plans were re-calculated with MC.

Results: Relative to FB, the total lung volume increased 86.8% in DIBH, while the gross tumor volume decreased 14.8%. MC revealed equally under- and over-dosage of the target for FB and DIBH, compared to AAA. For the Organs-At-Risk (OARs), DIBH reduced the mean heart dose by 25.5% (AAA) vs. 12.6% (MC), the total lung V_{5Gy}/V_{20Gy} by 9.0/20.0% (AAA) vs. 11.6/19.9% (MC).

Conclusions: MC calculations revealed (i) that DIBH compared with FB can significantly reduce the dose to the OARs even if the treatment planning is carried out with AAA, and (ii) inferior target dose coverage compared to AAA, irrespectively of FB and DIBH. The dose deviations were similar for FB and DIBH. The observed inferior target dose coverage relates therefore to the treatment planning algorithm rather than breathing technique.

Respiratory motion is a challenge during radiotherapy of Non-Small-Cell Lung Cancer (NSCLC) patients. Deep-Inspiration Breath-Hold (DIBH) is a method to diminish the uncertainty of breathing motion during radiotherapy for both lung, breast and Hodgkin lymphoma [1–4]. During DIBH, the lung is inflated, and the density of the lung parenchyma decreases, while the heart moves toward the back of the thorax, where the shape of the heart is affected of the inflated lungs. For some DIBH cases, the Gross Tumor Volume (GTV) can be displaced away from the radiosensitive spinal cord [1]. DIBH is a treatment method which may enable use of smaller treatment fields due to less tumor motion, consequently reducing dose to the adjacent healthy tissues and Organs-At-Risk (OARs).

Lung cancer GTVs are often situated in a region of large tissue heterogeneity where the accuracy of the dose calculation algorithm is critical to a precise evaluation of target dose coverage. Monte-Carlo (MC) dose calculations are able to simulate all ionization interactions present in a patient. The disadvantage with MC is the large computation time because of the many interaction histories required. Most commercial dose calculation algorithms utilize approximations to limit the computation time. Many commercial algorithms have issues to correctly account for changes of lateral electron scatter [5–7]. The dose calculation accuracy is thereby affected negatively, and not comparable with MC in heterogeneous geometries. The largest inaccuracies are usually noticed in the transition between materials of different densities. Lateral charged particle disequilibrium will be emphasized during DIBH, since the lung density decreases. The range of secondary electrons will

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increase resulting in a larger volume of disequilibrium and a broader penumbra at field boundaries [3,8].

The clinical benefit of DIBH for lung cancer patients have previously been evaluated in studies based on simple field technique and simplified calculation algorithms [9–13]. Due to the high amount of heterogeneities present in the lung region, there are limitations to these studies. Still, there are some studies presenting MC calculations [3,8,14–19] and measurement data [7,20] for lung treatments and dose delivered to the lungs. Most of these studies investigate conventional treatment techniques with static fields, and did not investigate the potential benefits of DIBH. However, the MC study by Wang et al. [15] presented a dosimetric evaluation for 5 lung cancer patients treated with intensity-modulated radiation therapy (IMRT), where one patient was treated with end-inspiration gating. They did however not assess the potential benefit of DIBH for this more complex treatment technique. This current study, including 18 patients, is the first DIBH MC study designed to obtain accurate assessment of the potential benefits of DIBH compared to Free-Breathing (FB) for volumetric-modulated-arc therapy (VMAT) and IMRT for locally advanced lung cancer. For this purpose, VMAT and IMRT treatment plans produced in a convolution–superposi tion based Treatment Planning System (TPS) were re-calculated using MC, comparing DIBH with FB.

Material and methods

Patient data

Eighteen locally advanced NSCLC patients scheduled for curative radiotherapy at Herlev Hospital, between December 2012 and July 2014, were enrolled. The patients were treated in FB with VMAT or IMRT in 33 fractions (fx), receiving a total dose of 66 Gy (2 Gy/fx, 5 fx/week). The treatments were delivered using Varian Clinac iX 2300 linear accelerators [21,22] (Varian Medical Systems, Palo Alto, CA) equipped with On-Board Imagers (OBI) capable of performing FB and DIBH cone-beam CT, using version 1.5 of the OBI software. Table 1 summarizes the patient characteristics.

Table 1
Summary of patient characteristics.

Patient characteristics	Number of patients (%) or median (min; max)
Median age	63 (48;75)
Gender	
Male	12 (67%)
Female	6 (33%)
Performance status	
0	17 (94%)
1	1 (6%)
Differentiating grade	
Adenocarcinoma	12 (67%)
Planocellular carcinoma	5 (27%)
Larce cell neuroendocrine carcinoma	1 (6%)
T-stage	
1	2 (11%)
2	2 (11%)
3	7 (39%)
4	7 (39%)
N-stage	
0	3 (17%)
1	3 (17%)
2	8 (44%)
3	4 (22%)
M-stage	
0	18 (100%)
Tumor location	
Upper lobe/middle lobe	15 (83%)
Lower lobe	3 (17%)
Primary tumor site	
Central	9 (50%)
Peripheral	3 (17%)
Chest wall	4 (22%)
Central/chest wall	2 (11%)
Mediastinal involvement	
Tumor	1 (6%)
Lymph node	5 (28%)
Tumor and lymph node	10 (55%)
No involvement	2 (11%)

Ethical considerations

The clinical protocol was approved by the Copenhagen Regional Committee on Health Research Ethics (protocol No. H-4-2012-066) and the Danish Data Protection Agency-(ID. nr.: 2007-58-0015/HEH.750.24-61). Every patient gave informed consent prior to inclusion.

Image acquisition

Prior to planning imaging, all patients were introduced during a 30 min training session to the DIBH procedure by a radiotherapist (RTT). The Varian Real-time Position Management (RPM) system, version 1.7 (Varian Medical Systems), integrated with the CT imaging system, was utilized to monitor the patients' respiration [23]. The patients were audio-visually guided during DIBH by using video goggles to achieve a reproducible inspiration level. During the training session, they were required to hold their breath at least 20 s at a reproducible patient-specific amplitude level and a gating window of 2–3 mm width.

All images were acquired in treatment position. The CT image protocol and details about the delineation of anatomical structures have previously been described by Ottosson et al. [21,24]. In brief, each patient was dual-CT scanned in a 16 slice Philips Brilliance CT Big Bore scanner, version 3.5.17001 (Philips Medical Systems, Cleveland, OH) (acquiring a 4-dimensional CT (4DCT) in FB and a normal CT in DIBH). Intra-venous contrast was administered to the patients during both 4DCT and DIBH CT imaging, for better contrast of nodal anatomy in the mediastinum. Each image set included the entire lung volume, starting from the top of the sixth cervical vertebrae. From the FB 4DCT an untagged image reconstruction and a Maximum Intensity Projection (MIP) image set were obtained [21]. Each patient was additionally scanned in a GEMINI TF 16 slice Big Bore PET/CT, version 2.3 (Philips Medical Systems) in order to diminish the delineation uncertainties in the CT.

Definition of target and organs at risk

The image sets were imported and co-registered in the Eclipse TPS, version 10 (Varian Medical Systems). Delineations of anatomical structures were performed according to standard protocol by only one experienced oncologist (JLA or SB) on all image sets for that patient [21]. Contouring of the GTVs was performed in collaboration with an experienced radiologist using information from the co-registered MIP and PET/CT images. The delineated GTV was subsequently verified and corrected in all breathing phases. Residual structures such as the clinical target volume (CTV), the planning target volume (PTV), medulla, heart, esophagus, lung, healthy lung (the opposing lung from where the primary tumor is located) were additionally delineated solely by the oncologist, whereas CT radiographers semi-automatically delineated the body contour.

Treatment planning process

All treatment plans were created using the Anisotropic-Analytical-Algorithm (AAA) dose calculation algorithm in Eclipse by one treatment planner (CL), experienced in lung cancer, in order

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