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Adaptive radiotherapy

Anatomical landmarks accurately determine interfractional lymph node shifts during radiotherapy of lung cancer patients

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ABSTRACT

Background and purpose: Low contrast in the cone-beam computed tomography (CBCT) scans hampers fast online evaluation of interfractional changes in the lymph node position on a daily basis. In this study we have investigated whether high-contrast anatomical landmarks in the vicinity of the nodes may be used as surrogates for the lymph node positions.

Materials and methods: Forty lung cancer patients were treated with an online CBCT-based setup strategy involving soft-tissue match on the primary tumor. One hundred and sixteen lymph nodes were delineated separately on the planning-CT scans and categorized according to the lymph node stations. Five anatomical landmarks were selected as surrogate structures and assigned to the individual nodes. In addition, the carina was delineated. Registrations between the planning-CT and the daily CBCTs were performed retrospectively and positional deviations between the nodes and the surrogate structures or the carina were registered.

Results: The mean displacement between lymph nodes and surrogate structures was 1.6 mm with systematic/random errors of 0.7/0.7 mm, significantly smaller than the mean displacement between nodes and the carina.

Conclusions: The position of the lymph nodes can be evaluated using selected anatomical landmarks on a daily basis using CBCT.

Survival rates for lung cancer patients treated with radiotherapy (RT) remain low partly due to the high rates of local recurrence [1,2]. It has been shown that the local control rate may be improved by increasing the RT dose [3–5]. However, this requires high precision in the daily RT delivery, in order to minimize margins and avoid unacceptable normal tissue toxicity [6,7].

Daily online image-guided setup reduces the systematic and random errors and thereby the margins [8]. The online setup can either be based on anatomical landmarks [9–11] or based on soft-tissue tumor matches [8,12–14]. In some patients, large systematic changes in the position of the primary tumor or lymph nodes are seen on the daily CBCTs [15–17]. The volume of the primary tumor and the lymph nodes may change independently, introducing positional changes [12,18–20]. Additionally, normal tissue changes, e.g. appearance of an atelectasis, leads to geometrical changes of the tumor and lymph nodes [13,15,21]. Adaptive replanning [22] has been introduced to handle large deviations not accounted for by the applied standard margins. This requires observation of positional changes of both tumor and lymph nodes during the RT course. The primary tumor is often visible on kV-CBCT, whereas the low contrast in the mediastinum makes it difficult to visualize the lymph nodes. Anatomical landmarks such as the carina can be used as surrogate structures for fast online evaluation. The interfractional positional changes of lymph nodes have been studied in a few reports [13,18,19] indicating that overall, the carina is a good surrogate for the lymph node positions. However, the correlation to the individual nodes has not been investigated.

The aim of the present study was, to find a reliable strategy to evaluate the position of the lymph nodes online by CBCT, in the setting of daily image-guided adaptive RT (ART) for lung cancer. The daily CBCTs were used for the analysis due to the large number of scans. However, as the contrast of the CBCTs is inferior to the CT-contrast, a validation study using CT–CT registrations underlies the study.

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Materials and methods

Patients

A total of 40 lung cancer patients with malignant lymph nodes were treated in our institution with radical chemo-RT between April and November 2013 (Table 1). The patients with non-small cell lung cancer (NSCLC) received 3 cycles of cisplatin/carboplatin and vinorelbine concomitant with 60–66 Gy in 30–33 fractions (F), 5 F/week while patients with small-cell lung cancer (SCLC) received 4 cycles of cisplatin/carboplatin and etoposide concomitant with 45 Gy in 30 F, 10 F/week. All tumors were pathologically proven.

Pre-treatment image acquisition and contouring

All patients underwent a free-breathing ^{18}FDG PET-CT planning scan with 3 mm slice spacing and a pixel size of 1×1 mm^2 for the CT-scan. The patients were positioned with both arms above the head in a standard or an individualized immobilisation device. The CT-scan was performed with i.v. contrast as a time-resolved 4D-scan and the midventilation phase was selected for delineation of normal tissue and for treatment planning. The gross tumor volumes of the tumor, GTV-T, and the lymph nodes, GTV-N, were delineated using the maximum intensity projection thus accounting for respiratory tumor motion [23,24]. The GTVs were expanded to clinical target volumes (CTVs) by an isotropic 5 mm margin. In addition to delineation of the GTV-N, the nodes were delineated separately [25]. When two small nodes were located within 2 cm, they were gathered in one structure. Conglomeration of nodes extending to more than one lymph node station, were divided into separate structures.

For each patient, two additional 4D CT-scans were acquired during RT approximately at fractions ten and twenty. Target and normal tissue structures were delineated on the midventilation phase of all additional CT-scans based on both a rigid and a daemons-based deformable transfer from planning-CT [26] (SmartAdapt, Varian Medical Systems) followed by manual correction by an experienced radiation oncologist.

Table 1
Patient characteristics.

Characteristic	SCLC = 14	NSCLC = 26
Mean age (range)	66.5 (47–81) years	63.4 (50–84) years
Gender		
Male	6	18
Female	9	17
Median GTV-T size (range)[a]	22 (3–255) cm^3	58 (1–350) cm^3
Median GTV-N size (range)[a]	25 (5–277) cm^3	17 (1–119) cm^3
T-stage		
T0	1	3
T1	4	4
T2	4	7
T3	2	2
T4	3	10
N-stage		
N1	2	1
N2	5	19
N3	7	7
M-stage		
M1[b]	0	2
Primary tumor location		
Upper lope	7	12
Middle lope	0	1
Lower lope	3	6
Upper + lower lope	3	3
Middle + lower lope	0	1
Lymph node location		
Station 1	10	5
Station 2	4	3
Station 4	19	25
Station 5	3	4
Station 6	3	3
Station 7	6	11
Station 10	4	8
Station 11	3	4
Station 12	0	1

In one patient, GTV-T disappeared before RT and only GTV-N was treated. Only one lymph node was located in station 12. This node was omitted from the analysis.
[a] The volume of GTV-T and GTV-N included respiratory motion.
[b] All radically treated single metastases. Brain ($N = 1$) and subcutaneous ($N = 1$).

Delineation of surrogate structures

Anatomical landmarks visible on CBCT within 2 cm from the lymph nodes were delineated on the midventilation phase of the planning-CT and the additional CT-scans and assigned as surrogate structures for evaluation of the nodes. Five anatomical landmarks were used as surrogate structures and each lymph node station was assigned a surrogate structure. These structures, shown in Fig. 1, were individualized depending on the CC-extension of the nodes. The cranial part of the thoracic vertebrae and the trachea was delineated for nodes in station 1 or 2. The extension in the CC-direction was chosen as the extent of the node, at least one vertebra. For nodes in station 4, the carina was delineated. The structure included at least 1 cm of the main bronchi and the trachea and extended in the CC-direction to the CT-slice of the most cranial/caudal position of the node. Lymph nodes in station 5: similar to station 4 with the addition of part of the descending aorta defined in the CC-direction by the extension of the node. Lymph nodes in station 6: the aortic arc defined caudally by the extension of the node. Nodes in station 7: the caudal part of the thoracic vertebrae. Nodes in station 10 + 11: The ipsilateral hilum including the bronchus and the malignant lymph node. The hilum was defined by the boundary adjacent to lung tissue, whereas the mediastinal boundary was of no importance and thus arbitrary. Only the demarcation to the lung tissue was used for CBCT. In patients with multiple malignant lymph nodes, a surrogate structure was delineated for each node. In total, 80 surrogate structures were delineated, matching 116 nodes, as some nodes use the same structure. Furthermore, the carina was delineated in all patients for comparison to the assigned surrogate structures.

In-room imaging and soft-tissue match

A 3D CBCT-scan acquired with a kV On-Board Imager system (Varian Medical Systems) was used for daily image-guided patient setup. The axial field of view was 16 cm. The CBCT-scan was registered automatically to the planning-CT scan based on a GTV-T soft-tissue match. The radiation therapists (RTT) evaluated the registration and the resulting 3D-translational shifts and couch rotation were performed. For patients with systematic deviations in the position of the tumor or lymph nodes above a pre-set limit, adaptive re-planning was performed (Supplementary material).

Retrospective CBCT registration

Altogether, a total of 1233 CBCT-scans were available for analysis. The 3D CBCT-scans were retrospectively registered to the midventilation of the planning-CT scan for each patient using Offline Review (Varian Medical Systems). Rigid soft tissue registrations based on gray-scale values were performed. First, a registration on GTV-T using 3D-translational shifts as well as couch rotation was made to simulate the online match-situation. Hereafter, the couch rotation was fixed for each CBCT-scan. Then, a number of 3D soft-tissue registrations were performed using each lymph node structure and each surrogate structure for the