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Lung cancer

Comparison of anisotropic aperture based intensity modulated radiotherapy with 3D-conformal radiotherapy for the treatment of large lung tumors

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ABSTRACT

Purpose/objective(s): IMRT allows dose escalation for large lung tumors, but respiratory motion may compromise delivery. A treatment plan that modulates fluence predominantly in the transversal direction and leaves the fluence identical in the direction of the breathing motion may reduce this problem.

Materials/methods: Planning-CT-datasets of 20 patients with Stage I–IV non small cell lung cancer (NSCLC) formed the basis of this study. A total of two IMRT plans and one 3D plan were created for each patient. Prescription dose was 60 Gy to the CTV and 70 Gy to the GTV. For the 3D plans an energy of 18 MV photons was used. IMRT plans were calculated for 6 MV photons with 13 coplanar and with 17 noncoplanar beams. Robustness of the used method of anisotropic modulation toward breathing motion was tested in a 13-field IMRT plan.

Results: As a consequence of identical prescription doses, mean target doses were similar for 3D and IMRT. Differences between 3D and 13- and 17-field IMRT were significant for CTV Dmin (43 Gy vs. 49.1 Gy vs. 48.6 Gy; $p < 0.001$) and CTV D_{95} (53.2 Gy vs. 55.0 Gy vs. 55.4 Gy; $p = 0.001$). The D_{mean} of the contralateral lung was significantly lower in the 17-field plans (17-field IMRT vs. 13- vs. 3D: 12.5 Gy vs. 14.8 Gy vs. 15.8 Gy: $p < 0.05$). The spinal cord dose limit of 50 Gy was always respected in IMRT plans and only in 17 of 20 3D-plans. Heart D_{max} was only marginally reduced with IMRT (3D vs. 13- vs. 17-field IMRT: 38.2 Gy vs. 36.8 Gy vs. 37.8 Gy). Simulated breathing motion caused only minor changes in the IMRT dose distribution (~0.5–1 Gy).

Conclusions: Anisotropic modulation of IMRT improves dose delivery over 3D-RT and renders IMRT plans robust toward breathing induced organ motion, effectively preventing interplay effects.

Radiotherapy (with or without additional chemotherapy) remains the standard treatment for patients with advanced lung cancer. Stereotactic body radiotherapy (SBRT) is a common treatment technique, used successfully for patients with medically inoperable small volume lung cancer [1,2]. Results of multimodal treatment of patients with treatment volumes that are large relative to normal lung tissue are still not satisfactory. Both local and distant controls pose a major problem [3]. It is already evident that high-dose radiotherapy increases local control and cure rates. Intensity modulated radiotherapy (IMRT) allows to select optimal beam directions and their combination, which allows dose escalation without excessive toxicities, including those to the spinal cord, the esophagus, and lungs. A specific problem for IMRT of lung tumors is respiratory motion. Lung tumors and OAR can change their position in the cranio-caudal and anterior–posterior direction by up to 2 cm as a function of the breathing cycle [4]. As this motion can result in alterations in target and normal tissue volume definitions, target margins and the entire dose distribution (due to "interplay" effects when an inhomogeneous fluence is projected sequentially onto a moving object), interventions to reduce the impact of intratreatment organ motion are necessary [5]. A treatment plan that modulates fluence predominantly in the transversal directions and leaves fluence identical in the longitudinal patient direction i.e. the direction of the breathing motion (anisotropic modulation) might reduce this problem, while it might still improve dose conformality over 3D-conformal radiotherapy and thus might enable dose escalation. The favorable features of the aperture based technique include faster optimizations, fewer degrees of freedom, and the avoidance of the degrading segmentation phase inherent in beamlet-based inverse planning. Moreover, if the apertures are related in a useful way to the anatomy of the patient, the possibility of simplifying the treatment verification presents itself [6]. In this study, we compared conventional 3D conformal radiotherapy treatment plans with anisotropic IMRT for patients with large volume lung cancer not suitable for SBRT and hypothesized, that the anisotropic technique is robust toward

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target movement and that with the implementation of this technique we can escalate the dose to the target, and at the same time reduce the dose to the OAR.

Methods and materials

CT-datasets of 20 patients with Stage I–IV non small cell lung cancer (NSCLC) formed the basis of this study. Specific patient characteristics are presented in Table 1.

The basis for 3D and IMRT plans were thin slice computer tomography (CT) scans acquired on a dedicated 8 slice CT simulator (Somatom Plus 4 Volume Zoom, Siemens®, 120 kV, 200 mAs/section, 10-mm thickness, 10-mm increment. 3D and IMRT plans were generated on PrecisePLAN© 2.03 for a Synergy© linac equipped with a multileaf collimator (leaf width 10 mm at isocenter) and a maximum dose rate of 600 MU/min (Elekta Oncology Systems, Crawley, UK).

The gross tumor volume (GTV) was defined as the gross mass demonstrated by planning CT images. The clinical target volume (CTV) was determined as the volume encompassing GTV, the regional lymph nodes, and an addition of a 10-mm margin. For comparative planning purposes, a planning target volume (PTV) was not used. Mean CTV and GTV sizes were 515 cm^3 and 342 cm^3, respectively (Table 1). GTV and CTV were contoured as non-overlapping volumes (CTV did not include GTV). Both lungs (right and left lung separately, including the healthy lung volume included in the CTV), heart and spinal cord were contoured as OAR. Two IMRT plans and one 3D plan were created for each of the 20 patients. Prescription dose was 60 Gy to the CTV and 70 Gy to the GTV. For the 3D plan, 3–6 beams, an energy of 18 MV photons and wedge filters were used. The margin between the CTV and the MLC was 0.5 mm. The 3D plans were planned to a total dose to 60 Gy (CTV plus GTV), followed by an external beam boost to a total dose of 70 Gy to the GTV (sequential 3D-Boost). IMRT plans were calculated with 6 MV an 18 MV photon energy in preliminary experiments. As expected based on previous publications, no significant differences in the results were observed, therefore only the 6 MV plans were used for the comparison [7]. For IMRT, two techniques were studied per beam energy: (a) 13 coplanar beams and (b) a 17 beam technique with 13 coplanar and 4 noncoplanar primary beam directions. Beam angles were arranged in a practical manner according to tumor and OAR position for the purpose of achieving maximal target coverage and optimal dose distributions (minor deviations from an isotropical setup). Instead of resorting to the rather complex full inverse-planning, where one has no control on segment shaping, our technique using PrecisePLAN is an extension of the conformal treatment planning technique where within each field beam eye view (BEV) a number of sub-field apertures are added.

Table 1
Patient characteristics.

	n (%)
Age (years)	
Median	68
Range	49–83
Gender	
Male	16 (80)
Female	4 (20)
Histological subtype	
Adenocarcinoma	7 (35)
Squamous cell cancer	13 (65)
Stage I/II	4 (20)
Stage IIIA	5 (25)
Stage IIIB	8 (40)
Stage IV	3 (15)
GTV (cm^3)	
Median	342
Range	53–649
CTV (cm^3)	
Median	515
Range	82–1114

Abbreviations: NSCLC, non-small cell lung cancer; CTV, clinical target volume; GTV, gross tumor volume.
Data is presented as number of patients (*n*), with percentages in parentheses.

Initially a set of segments including the entire target volume was generated manually, followed by segments that included the target volume only partially and excluded the OAR's. The smaller apertures are designed to irradiate the tumor, while mutually sparing OARs that intrude into the target region in the BEV. A 3D dose display overlaid on the BEV simplifies and guides the manual segmentation process (Figure 1). This method leads to a relatively small number of comparatively large sized apertures and allows the planner to intentionally shape the segments for less longitudinal fluence modulation. In the next step, constraint-driven inverse optimization of segment weights based on a Cimmino algorithm was performed. Each field is individually weighted, allowing all of the fields to contribute to the total dose distribution according to the beam geometry.

Six 13-field IMRT plans were selected to assess robustness of anisotropically modulated IMRT toward motion. To simulate random breathing motion during treatment, new plans were created with the isocenters of all segments being moved randomly between 1 and 10 mm in craniocaudal direction. Dose calculation was performed using the Collapsed Cone (CC) algorithm implemented in Oncentra Masterplan© (Nucletron BV, Veenendaal, Netherlands).

Plan comparison was based on absolute dose statistics for GTV, CTV, lung tissue, heart, and spinal cord. Quantitative parameters of dose–volume relationships such as D_{95} (the relevant minimum dose), D_{mean}, D_{max} for GTV and CTV and D_{mean}, D_{max}, $D_{30\%}$ and $D_{60\%}$ (dose exceeded by 30%/60% of the volume) for lung tissue, spinal cord, and heart were selected for comparison. For CTV, V_{110} and for GTV the highest dose applied to more than 1 cc of the target volume (to assess the magnitude of clinically relevant dose peaks) and for lung tissue the V20 for the whole lung was recorded. Dose profiles and DVHs were compared between 3D- and IMRT plans. Group differences were assessed using the exact Wilcoxon signed rank test. All testing was two-tailed, with $p < 0.05$ considered statistically significant. Statistical procedures were performed using the IBM SPSS Statistics program (version 18, SPSS Inc., Chicago, IL).

Results

As a consequence of identical prescription doses and an emphasis on target coverage, mean target doses were similar for 3D and IMRT (Table 2). Wilcoxon signed rank tests showed that the differences between 3D and 13- and 17-field IMRT, were significant for CTV Dmin (43 Gy vs. 49.1 Gy vs. 48.6 Gy; $p < 0.001$) and CTV D_{95} (53.2 Gy vs. 55.0 Gy vs. 55.4 Gy; $p = 0.001$). GTV- and CTV DVH-metrics were therefore anchored at very similar values. Plan characteristics are therefore mainly based on OAR DVH-metrics.

There was no significant difference in D_{mean} for the ipsilateral lung between 3D and the 13- and 17-field IMRT plans (23.1 Gy vs. 19.5 Gy vs. 20.5 Gy; p = n.s). There were significantly better results for $D_{30\%}$ (3D vs. 13- vs. 17-field IMRT: 39.6 Gy vs. 37 Gy vs. 35.3 Gy; $p < 0.03$) in favor of the IMRT plans.

The V20 mean values for both treatment techniques were above 20% (3D vs. 13- vs. 17-field IMRT: 38.8 Gy vs. 36.3 Gy vs. 33.5 Gy), but the values of the 3D plans were higher than the values of the