Influence of Calculation Algorithm on Dose Distribution in Irradiation of Non-Small Cell Lung Cancer (NSCLC)

Collapsed Cone Versus Pencil Beam

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Purpose: The influence of two different calculation algorithms („pencil beam" [PB] versus „collapsed cone" [CC]) on dose distribution, as well as the dose-volume histograms (DVHs) of the planning target volume (PTV) and the organs at risk was analyzed for irradiation of lung cancer.

Material and Methods: Between 10/2001 and 02/2002 three-dimensional treatment planning was done in ten patients with lung cancer (Helax, TMS®, V.6.01). The PTV, the ipsilateral lung (IL) and the contralateral lung (CL) were defined in each axial CT slice (slice thickness 1 cm). Dose distributions for three-dimensional multiple-field technique were calculated using a PB and a CC algorithm, respectively. Normalization was in accordance with ICRU 50. The DVHs were analyzed relating the minimum, maximum, median and mean dose to the volumes of interest (VOI).

Results: Median PTV amounted to 774 cm^3. Minimum dose within the PTV was 67.4% for CC and 75.6% for PB algorithm ($p = 0.04$). Using the CC algorithm, only 76.5% of the PTV was included by the 95% isodose, whereas 90.1% was included when the PB algorithm ($p = 0.01$) was used. Median volume of IL amounted to 1 953 cm^3. Mean dose to IL was 43.0% for CC and 44.0% for PB algorithm ($p = 0.02$). Median volume of IL within the 80% isodose was 19.6% for CC and 24.1% for PB algorithm ($p < 0.01$). Median volume of CL amounted to 1 847 cm^3. Mean dose to CL was 17.4% for CC and 18.1% for PB algorithm ($p < 0.01$). Volume of CL within the 80% isodose was 3.3% for CC and 4.1% for PB algorithm ($p = 0.03$).

Conclusion: The CC and PB calculation algorithms result in different dose distributions in case of lung tumors. Particularly the minimum dose to the PTV, which may be relevant for tumor control, is significantly lower for CC. Since it is generally accepted that the CC algorithm describes secondary particle transport more exactly than PB models, the use of the latter should be critically evaluated in the treatment planning of lung cancer.

Key Words: Lung cancer · Radiotherapy · Calculation algorithms · Collapsed cone algorithm · Pencil beam algorithm

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Der Einfluss des Rechenalgorithmus auf die Dosisverteilung bei der Bestrahlung des nichtkleinzelligen Bronchialkarzinoms (NSCLC). Collapsed Cone versus Pencil Beam

Ziel: Der Einfluss zweier unterschiedlicher Rechenalgorithmen („pencil beam" [PB] versus „collapsed cone" [CC]) auf die Dosisverteilung sowie die Dosis-Volumen-Histogramme (DVH) des Planungszielvolumens (PTV) und der Risikoorgane wird für die Bestrahlung des Lungenkarzinoms untersucht.

Material und Methodik: Zwischen 10/2001 und 02/2002 wurde bei zehn Patienten mit Bronchialkarzinom eine dreidimensionale Bestrahlungsplanung durchgeführt (Helax, TMS®, V.6.01). Das PTV, die ipsilaterale Lunge (IL) und die kontralaterale Lunge (CL) wurden in jeder axialen CT-Schicht definiert (Schichtdicke 1 cm). Die Dosisverteilung für eine Mehrfeldertechnik wurde zunächst unter Verwendung des PB-Algorithmus optimiert. Anschließend wurde die Dosisverteilung der sich dabei ergebenden Bestrahlungspläne unter Beibehaltung der Feldparameter mittels des CC-Algorithmus erneut berechnet. Die Dosis wurde gemäß ICRU 50 normiert. Die DVH von PTV, IL und CL wurden analysiert.

Ergebnisse: Das PTV betrug im Median 774 cm^3. Die minimale Dosis im PTV war 67,4% für den CC- und 75,6% für den PB-Algorithmus ($p = 0{,}04$). Unter Verwendung von CC wurden lediglich 76,5% des PTV von der 95%-Isodose umschlossen, während dies unter Verwendung des PB bei 90,1% der Fall war ($p = 0{,}01$). Das mediane Volumen der IL war 1 953 cm^3. Die mittlere Dosis in der IL betrug für den CC-Algorithmus 43,0% bzw. für den PB-Algorithmus 44,0% ($p = 0{,}02$). Das Volumen der IL innerhalb der

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80%-Isodose betrug 19,6% für den CC- und 24,1% für den PB-Algorithmus ($p < 0{,}01$). Das mediane Volumen der CL lag bei 1 847 cm³. Die mittlere Dosis im Bereich der CL betrug 17,4% für den CC- und 18,1% für den PB-Algorithmus ($p < 0{,}01$). Das Volumen der CL innerhalb der 80%-Isodose war 3,3% für den CC- und 4,1% für den PB-Algorithmus ($p = 0{,}03$).
Schlussfolgerung: Die Berechnung der Dosisverteilung mit dem CC- bzw. dem PB-Algorithmus führt bei gleicher Feldkonfiguration zu erheblich unterschiedlichen Ergebnissen. Insbesondere die sich dabei ergebende Minimaldosis im Bereich des PTV, welche für die Tumorkontrolle relevant sein kann, ist beim CC-Algorithmus signifikant niedriger. Da der CC-Algorithmus die tatsächlichen Streuungsverhältnisse im Gewebe unterschiedlicher Dichte genauer berücksichtigt als der PB-Algorithmus, sollte die Verwendung des PB-Algorithmus für die Bestrahlungsplanung des Bronchialkarzinoms sehr kritisch beurteilt werden.

Schlüsselwörter: Bronchialkarzinom · Radiotherapie · Rechenalgorithmen · Collapsed-Cone-Algorithmus · Pencil-Beam-Algorithmus

Introduction

Lung cancer is the most common cancer in the world and we expected about 375,000 new cases in Europe for 2000 [21]. Since only 20–30% of patients with non-small cell lung cancer (NSCLC) are suitable for curative surgery, primary radiotherapy plays an important role in therapy of NSCLC. In the past, the results achieved with conventional external-beam radiotherapy were poor [11]. In contrast to conventional radiotherapy, three-dimensional conformal radiotherapy (3DRT) based on a three-dimensional treatment planning system (3DPS) provides the possibility to deliver higher radiation doses to the tumor simultaneously sparing normal tissues [2, 5, 7, 9, 13, 15, 16, 20]. The advantage of 3DPS is not only to optimize the treatment technique but also to take tissue inhomogeneities into account for dose calculation. The calculation models currently used by most of the commercial 3DPS are pencil beam (PB) algorithms as well as superposition/convolution algorithms. The purpose of this paper was to analyze the influence of different algorithms on dose distributions in radiotherapy of NSCLC.

Material and Methods

Ten consecutive patients (nine male, one female; median age 64.9 years) receiving definitive radiotherapy because of NSCLC were studied. The tumor was located right in six patients and left in four. All patients were scanned using computed tomography (CT). The following volumes of interest (VOI) were defined in each axial CT slice:

- planning target volume (PTV): including the tumor and the ipsilateral hilar and mediastinal lymph node region including a margin to encompass subclinical disease and treatment-related uncertainties like patient movements, setup displacements and organ movements;
- the volume of the ipsilateral lung (IL);
- the volume of the contralateral lung (CL).

Treatment planning was done by a three-dimensional planning system (Helax, TMS®, V.6.01) using 18-MV photon beams to be delivered by a PRIMUS (Siemens) linear accelerator. A conformal multiple-beam technique was planned for each patient using a PB algorithm. Number of beams, beam angles, wedges and position of collimator leaves arranged in "beam's eye view" technique were individually selected to encompass the PTV as conformal as possible. Subsequently, each treatment plan was recalculated using a point kernel model, which is implemented in the TMS® in an analytical collapsed

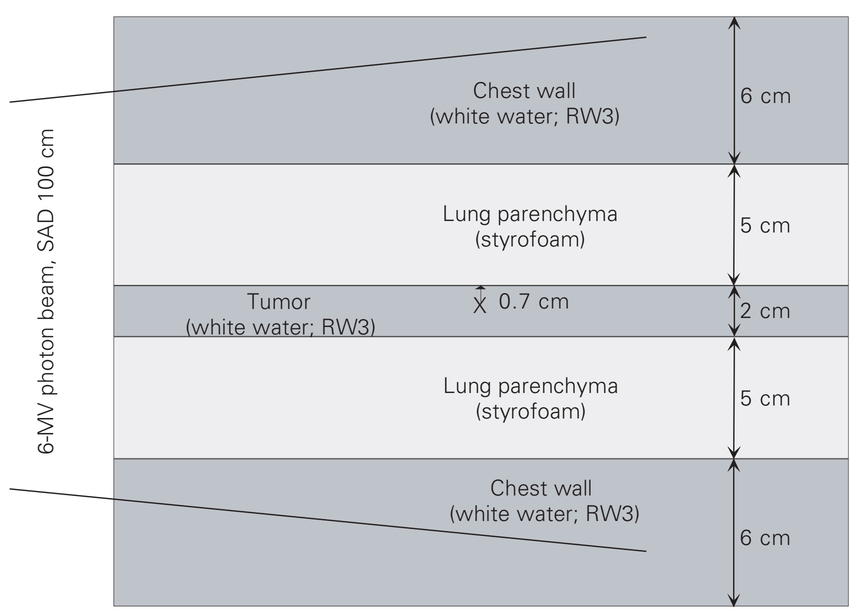

Figure 1. Schematic illustration of the lung phantom. The outer dimensions of the phantom are 30 × 30 × 24 cm. The position of ionization chamber measurement (point A) was at 150 mm depth and is marked by X.

Abbildung 1. Schematische Darstellung des Lungenphantoms. Die Ausdehnung beträgt 30 × 30 × 24 cm. Die Position der Ionisationskammer für die Messung (Punkt A) lag in 150 mm Tiefe und ist mit X markiert.

Figure 2. Exemplary dose distribution in an axial slice calculated by the pencil beam algorithm. In the calculated dose distribution the 20% (1), 40% (2), 60% (3), 80% (4), 90% (5), 95% (6), and 100% (7) isodose lines are displayed. PTV: planning target volume.

Abbildung 2. Exemplarische Dosisdarstellung in einer axialen Schicht, berechnet mit dem Pencil-Beam-Algorithmus. Dargestellt sind die 20%- (1), 40%- (2), 60%- (3), 80%- (4), 90%- (5), 95%- (6) und 100%-Isodosen (7). PTV: Planungszielvolumen.

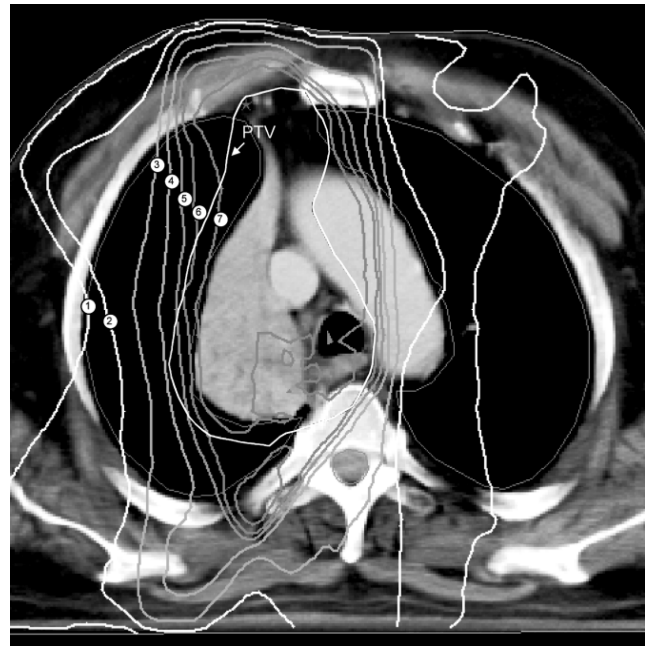

Figure 3. Exemplary dose distribution in an axial slice calculated by the collapsed cone algorithm. In the calculated dose distribution the 20% (1), 40% (2), 60% (3), 80% (4), 90% (5), 95% (6), and 100% (7) isodose lines are displayed. PTV: planning target volume.

Abbildung 3. Exemplarische Dosisdarstellung in einer axialen Schicht, berechnet mit dem Collapsed-Cone-Algorithmus. Dargestellt sind die 20%- (1), 40%- (2), 60%- (3), 80%- (4), 90%- (5), 95%- (6) und 100%-Isodosen (7). PTV: Planungszielvolumen.

cone (CC) approach. The dose-volume histograms (DVHs) of VOI were calculated. Normalization was in accordance with ICRU 50, the normalization point was the same for both calculation algorithms. Grid size of dose matrix geometry was 2.5 mm for dose calculation.

Phantom measurements were implemented to validate the planning system. A special phantom was designed for this study (Figure 1). It was constructed to model the physical characteristics of a solid tumor arising at the border of lung parenchyma. It consists of solid white water (RW3) and styrofoam. The geometry characteristics and density of the phantom were inserted into the planning system. The isocenter was located at point A at 150 mm depth in the phantom. Dose at point A was calculated for a 20 × 20 cm field for 18-MV photons using the PB and the CC algorithm. Additionally, an ionization chamber measurement was performed at point A. The phantom was irradiated by 100 monitor units using 18-MV photons.

The statistical significance of comparing CC and PB algorithm was determined using the t-test for dependent samples. Differences were reported to be statistically significant at $p \leq 0.05$. Statistical analysis was performed using STATISTICA (Kernel-Version 5.5).

Results

Calculation Algorithm

The dose distribution for PB and CC algorithm in an axial slice is shown exemplarily in Figures 2 and 3. Although the same field geometry was used, the calculated dose distributions in the target and the surrounding tissues clearly differed depending on calculation algorithm. This difference was most apparent at the air-tissue boundary resulting in a reduced dose to the PTV.

The number of monitor units required to deliver the prescription dose averaged 185.2 for CC algorithm and 182.5 for PB algorithm ($p < 0.01$). As a consequence of the lower number of monitor units the dose at the reference point calculated by the PB algorithm was 98.4% (95.7–99.8%) compared to the dose delivered by the monitor units calculated by the CC algorithm ($p < 0.01$). The lower number of monitor units calculated by the PB algorithm was taken into account for the analysis. The dose values were corrected by a reducing factor. The reducing factor was defined as ratio of number monitor units calculated by PB and CB algorithm.

Median PTV was 774 cm^3 (222–1,271 cm^3). Minimum PTV dose averaged 67.4% for CC and 75.6% for PB algorithm ($p = 0.04$). Insignificant differences were found for the maximum, median, and mean.

Table 1. Dose to planning target volume (PTV). CC: collapsed cone; PB: pencil beam.

Tabelle 1. Dosis im Planungszielvolumen (PTV). CC: „collapsed cone"; PB: „pencil beam".

	CC	PB	P-value
	Dose in % (standard deviation)		
Minimum	67.5 (10.0)	75.6 (13.7)	0.04
Maximum	107.0 (6.0)	107.7 (6.7)	0.3
Median	99.2 (1.8)	99.4 (3.0)	0.8
Mean	98.1 (2.2)	99.2 (3.2)	0.2
Isodose	**Volume of PTV in % (standard deviation)**		
100%	43.8 (17.9)	58.9 (24.4)	0.04
95%	76.5 (13.1)	90.1 (9.9)	0.01
90%	90.2 (8.2)	97.0 (2.4)	0.02
80%	97.6 (2.1)	98.3 (1.6)	0.3

Table 2. Dose to ipsilateral lung (IL). CC: collapsed cone; PB: pencil beam.

Tabelle 2. Dosis im Bereich der ipsilateralen Lunge (IL). CC: „collapsed cone"; PB: „pencil beam".

	CC	PB	P-value
	Dose in % (standard deviation)		
Minimum	1.4 (1.0)	3.0 (0.8)	0.01
Maximum	103.3 (2.8)	105.1 (3.7)	0.08
Median	38.2 (11.5)	35.7 (13.5)	0.04
Mean	43.0 (8.7)	44.0 (8.5)	0.02
Isodose	**Volume of IL in % (standard deviation)**		
100%	3.1 (3.2)	8.7 (7.4)	0.03
80%	19.6 (9.0)	24.1 (8.1)	0.01
60%	32.9 (8.8)	33.8 (8.2)	0.25
40%	49.2 (11.7)	48.5 (12.3)	0.59
20%	65.1 (11.8)	62.1 (11.8)	0.01

Using CC versus PB algorithm, an average of 76.5% versus 90.1% of the PTV was included by the 95% isodose (p = 0.01), and 90.2% versus 97.0% of the PTV by the 90% isodose (p = 0.02), respectively (Table 1).

Median volume of IL was 1 953 cm^3. Mean dose to IL was 43.0% for CC and 44.0% for PB algorithm (p = 0.02). Significant differences between the algorithms were found for high isodose levels. Volume of IL within the 80% isodose was 19.6% for the CC and 24.1% for the PB algorithm (p < 0.01; Table 2).

Median volume of CL was 1 847 cm^3. Mean dose to CL was 17.4% for CC and 18.1% for the PB algorithm (p < 0.01). Volume of CL within the 80% isodose was 3.3% for CC and 4.1% for PB algorithm (p = 0.03; Table 3).

Phantom Measurements

The dose measured by ionization chamber was 0.879 Gy. The dose calculated by PB algorithm was 0.980 Gy and by CC algorithm 0.869 Gy. PB algorithm overestimates the dose at point A by 11.4%, whereas there was only a difference of 1.2% between the measured dose and the dose calculated by CC algorithm.

Discussion

In the past, several studies compared the treatment technique devised with conventional planning techniques to those devised with 3DRT [2, 5, 13]. These analyses showed that conformal radiotherapy allows to increase radiation dose and to ensure complete coverage of the tumor volume. Additionally, 3DPSs lead to an improved quantification of doses resulting in a more precise dose prescription to the tumor and a better definition of normal tissue tolerances in terms of DVHs [6, 18, 19, 23]. When doses are quantified, it must be considered that these are depending on the algorithm used for dose calculation. The 3DPS contains inhomogeneity correction algorithms to convert dose calculation in a homogeneous medium to the individual patient-related situation with tissue inhomogeneities. Most inhomogeneity correction algorithms are semi-empirical and accurate for only a limited set of simplified geometries [6]. While the effect of inhomogeneities on the primary photon fluence is mostly well predicted, their influence on the dose delivered by scattered radiation is often approximated in a less accurate way. Therefore, calculation errors have to be expected for many clinical situations [10, 24].

Table 3. Dose to contralateral lung (CL). CC: collapsed cone; PB: pencil beam.

Tabelle 3. Dosis im Bereich der kontralateralen Lunge (CL). CC: „collapsed cone"; PB: „pencil beam".

	CC	PB	P-value
	Dose in % (standard deviation)		
Minimum	0.9 (0.5)	2.0 (0.6)	0.01
Maximum	100.6 (4.3)	102.4 (4.1)	0.12
Median	11.3 (4.8)	12.3 (5.3)	0.13
Mean	17.4 (5.6)	18.1 (5.5)	< 0.01
Isodose	**Volume of CL in % (standard deviation)**		
100%	0.4 (0.4)	0.9 (0.6)	0.04
80%	3.3 (2.5)	4.1 (2.8)	0.03
60%	6.3 (3.9)	6.7 (4.2)	0.19
40%	10.7 (6.7)	9.8 (6.2)	0.01
20%	27.2 (9.2)	30.0 (9.9)	0.2

Today, it is generally accepted that Monte Carlo algorithms lead to the most accurate dose calculation in radiotherapy [8, 18], because they automatically include all physical interaction processes which can occur within inhomogeneous tissues. However, due to a large demand of computational power Monte Carlo algorithms were not in widespread use for clinical treatment planning in the past.

Instead, 3DPS of the last generation generally used PB algorithms for dose calculation. The clinical studies evaluating the benefit of 3DRT or correlating lung complication like pneumonitis with dose distributions mostly used PB or even less accurate algorithms [4, 17, 19]. The implementation of the PB model in the TMS® principally follows reference [1]. Primary and scattered dose components are treated separately. While primary dose is calculated using an equivalent path length approach, lateral inhomogeneities are not taken into account. As a consequence, the dose calculation yields precise results as long as there is lateral charged particle equilibrium. But this condition fails for irradiation of tumors near air cavities like head and neck cancer and lung cancer. As a result, the dose at the lateral interface of tumor and low-density tissue is overestimated by the PB algorithm [12]. Verellen et al. [22] reported an overestimation of the PTV dose by 9% at the boundary of an air cavity in a head and neck cancer treatment. Linthout et al. [14] found a 10% overestimation of the dose in the PTV at the boundary with low-density tissue for head and neck radiotherapy. Engelsman et al. [6] used a phantom for simulating the situation of irradiation of lung cancer. The dose at the 95% isodose level, as calculated with a PB algorithm for 15-MV photons, was actually 21.2% lower when measured in the phantom. Seen from this angle, the results of the studies using PB algorithms for correlation of tumor control probability and normal tissue complication probability with dose distribution should be considered critically.

Because of the limitations of the PB algorithms some 3DPS of the newer generation implemented point kernel-based models like the CC approach. In this calculation algorithm the point kernels are discretized into a set of coaxial cones of equal solid angle. All energy released into the cones is rectilinearly transported, attenuated, and deposited in volume elements along the cone axis, i.e., “collapsed” to the cone axis. During the energy transport process, attenuation and absorption are scaled by the local electron density. So this algorithm implicitly takes into account the tissue inhomogeneities present in the irradiated volume [1]. The CC algorithm is used as an alternative to the Monte Carlo method and achieves a compromise between speed and accuracy in dose calculation [3]. In a comparison of PB and CC algorithms for radiotherapy of head and neck cancer, the CC algorithm best estimates the buildup effect at the air-tissue boundary [14]. Butson et al. [4] verified the lung dose in an anthropomorphic phantom calculated by the CC algorithm. They described an up to 5% variation between doses calculated at the center and near the edge of the phantom and concluded the CC algorithm accurately calculates dose within inhomogeneous lung regions. To show the relevance of the used calculation algorithm in a clinical situation, we analyzed the influence of PB and CC algorithms on radiotherapy of lung cancer. Our data showed that the PB algorithm overestimates the dose at the boundary of the PTV when compared with a CC calculation. While 90.1% of PTV was covered by the 95% isodose when using the PB, only 76.5% of the PTV was covered when calculated by the CC algorithm although the same field parameters were used.

But what are the consequences for the clinical practice? An option to countervail the lower dose at the air-tissue boundary could be a technical modification, e.g., an enlargement of the beam sizes toward the lung. However, this should be done with caution. The knowledge of the dose-effect relation of an irradiation-induced pneumonitis based on the great clinical experience with treatment planning systems using the PB algorithm. An enlargement of beam sizes could result in an increased incidence of pneumonitis.

Conclusion

The calculation algorithm used for the clinical situation of radiotherapy of lung cancer influences the dose distribution especially for a PTV situated in or at the boundary of an air cavity. Due to their limitations, PB algorithms generally overestimate the dose at the border of the PTV in such situations. Measurements in inhomogeneous phantoms have verified that CC models are better suited to approximate the real dose distribution [4]. Therefore, the CC algorithm should be used for 3DRT of lung cancer. For clinical studies and the publication of their results it is not sufficient to describe the prescribed dose at the normalization point and the DVHs, but it is also necessary to describe the algorithm used for dose calculation as well.

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