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In silico comparison of photons versus carbon ions in single fraction therapy of lung cancer

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ABSTRACT

Purpose: Stereotactic body image guided radiation therapy (SBRT) shows good results for lung cancer treatment. Better normal tissue sparing might be achieved with scanned carbon ion therapy (PT). Therefore an in silico trial was conducted to find potential advantages of and patients suited for PT.
Methods: For 19 patients treated with SBRT, PT plans were calculated on 4D-CTs with simulated breathing motion. Prescribed single fraction dose was 24 Gy and OAR constraints used for photon planning were respected. Motion was mitigated by rescanning and range-adapted ITVs. Doses were compared to the original SBRT plans.
Results: CTV coverage was the same in SBRT and PT. The field-specific PTV including range margins for PT was 1.5 (median, 25–75% 1.3–2.1) times larger than for SBRT. Nevertheless, maximum point dose and mean dose in OARs were higher in SBRT by 2.8 (1.6–3.7) Gy and 0.7 (0.3–1.6) Gy, respectively. Patients with a CTV >2.5 cc or with multiple lung lesions showed larger differences in OAR doses in favor of PT.
Conclusions: Patients receive less dose in critical OARs such as heart, spinal cord, esophagus, trachea and aorta with PT, while maintaining the same target coverage. Patients with multiple or larger lesions are particularly suited for PT.

1. Introduction

Lung cancer is one of the leading medical problems worldwide with approximately 1.4 million deaths per year [1]. Surgery is usually the first choice in treating localized non-small cell lung cancer (NSCLC). However, in recent years stereotactic body-radiation therapy with photons (SBRT) showed very promising results, with high local control-rates of NSCLC [2–7].

Scanned particle therapy can produce sharp dose gradients with a finite range of the beam and can thus provide higher healthy tissue sparing. This reduces both side effects as well as the risk of secondary cancer [8]. Treatment of lung tumors with particles is still challenging due to interplay and radiological path length changes [9]. The latter can be substantial when dense tissue (e.g. the solid tumor mass) is replaced with low-density tissue (lung) due to motion.

Grutters et al. have performed a meta-analysis on comparison between photon, proton and carbon ions in treating NSCLC [4]. They found similar 5-year survival rates for SBRT, protons and carbon-ions (around 40%). However, the number of patients treated with particle therapy was low and they advise caution when interpreting the data. Also different fractionation schemes were used in the comparison. A more recent review was published by Kamada et al. [10] where they reported a high 3-year survival rate for single-fraction carbon-ions (76.9%), with no late treatment-related adverse effects. In comparison, SBRT had 55.8% 3-year survival rate, with 10–27% of patients exhibiting grade 3 treatment-related adverse effects. [6]. It is important to note that all of these studies used passive beam scattering, avoiding the problem of interplay between organ motion and scanning beam motion. On the other hand, active beam scanning can provide even better dose shaping which becomes essential in high dose single fractionation regimes. The effects of motion and motion mitigation techniques on scanned carbon ion dose distribution therefore need to be considered in a fair comparison of photons and carbon ions.

To evaluate potential advantages of active scanning with carbon ions (PT), an in silico comparison of simulated PT plans to SBRT plans actually delivered was conducted. Target coverage and a wide range of OAR doses were assessed both with and without simulated motion on time-resolved computed tomographies (4D-CTs).

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2. Methods

2.1. Patient data

Our study included 19 patients with in total 26 lesions that were actually treated with SBRT at the Champalimaud Centre for the Unknown, Lisbon (Portugal). The lesion size was 2.9 cc (median, 25–75% 1.4–9.7) and peak-to-peak motion was 3.1 mm (1.6–5.6). Three patients had two targets, one had five and the rest one. 13 lesions were right-sided, 12 were left-sided and one was located in right cardiophrenic space. An overview of tumor characteristics can be found in Table 1.

Two CTs were available for all patients. A planning CT was used for OAR delineation and SBRT planning. Target motion was estimated on a 4D-CT, consisting of 10 phases (0%–90%). Clinical target volumes (CTV) were delineated using a registered positron emission tomography (PET) scan.

The planning objectives were that 99% of planning target volume (PTV) must receive at least 24 Gy ($D_{99\%} \geqslant 24$ Gy) in a single fraction, while all OAR constraints as defined in the AAPM task group 101 report on stereotactic radiotherapy had to be respected [11].

2.2. Definition of target volumes

To account for range changes relevant for particles only, different PTV definitions were used for SBRT and PT, as shown in Fig. 1. Within this paper they will be named PTV_{SBRT} and PTV_{PT} for SBRT and PT, respectively.

In SBRT, the responsible clinician determined the maximum breathing motion of the CTV from the 4D-CT, hence creating an ITV. This ITV plus an additional 3 mm for setup uncertainty yielded the PTV_{SBRT}.

PTV_{PT} was constructed following principles from Graeff et al. [12]. Each beam has a unique PTV_{PT}. For setup uncertainty margins of 3 mm laterally and 1 mm in beam's eyes view (BEV) were used on the CTV. Afterwards a water-equivalent path length ITV (WEPL-ITV) was build, using transformation maps from the B-Spline deformable registration of the 4D-CT data [13]. Additional 2 mm + 2% proximal and distal margins were added in BEV to account for uncertainty from Hounsfield units to water equivalent path length conversion.

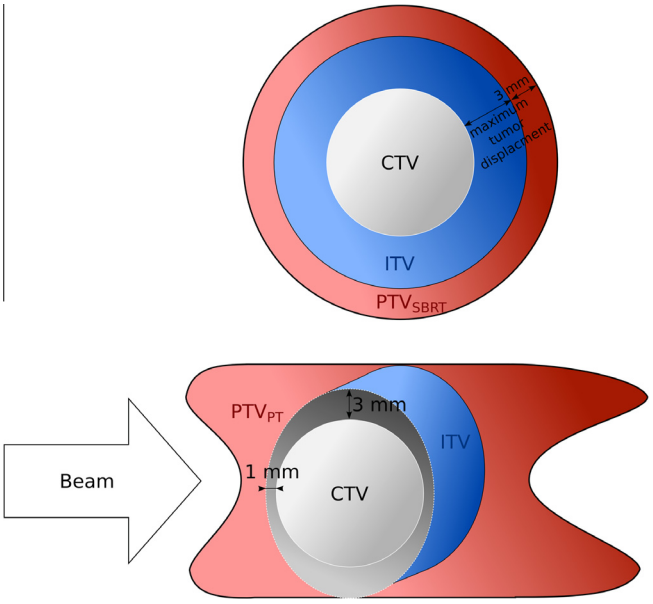

Fig. 1. Different PTV definitions for SBRT (PTV_{SBRT}) and PT (PTV_{PT}). For PTV_{SBRT} isotropic margins of 3 mm plus maximum tumor displacement due to breathing were used on the CTV; for PTV_{PT} margins of 3 mm laterally and 1 mm in beam's eye view were used and then range-ITV was constructed with 2 mm + 2% range margins added for PTV_{PT} in the end-inhale phase.

Table 1
Patient characteristics showing lesion locations, stages, peak-to-peak motions, and volumes of corresponding CTV, PTV_{SBRT} and PTV_{PT} (given as range).

Patient	Lesion number	Lesion location	Stage	Peak-to-peak motion (mm)	Volume (cc)		
					CTV	PTV_{SBRT}	PTV_{PT}
1	1	LSL	IIa	4.8	36	100	143.0–193.9
2	2	LSL	Ia	3.1	1.6	7.7	25.8–32.3
3	3	IRL	IV	12	2.3	12	25.2–39.1
3	4	RCS	IV	11.8	0.4	6.6	8.4–8.7
4	5	RSL	Ia	0.5	6.9	25	28.9–38.2
5	6	ILL	IV	4.4	2.4	15	0.0–19.2
6	7	ILL	IV	7.5	1.4	7.7	34.3–36.8
7	8	RSL	IV	3.9	16	40	62.6–76.5
8	9	ILL	IV	0.6	139	261	44.4–251.7
8	10	LSL	IV	2	9.2	35	242.3–251.7
9	11	IRL	IV	3.4	10	38	54.4–59.9
9	12	ILL	IV	2.8	14	46	44.1–47.0
10	13	ILL	IV	5.8	3.8	17	23.4–31.2
10	14	RSL	IV	0.8	4.3	18	26.9–30.3
10	15	LSL	IV	3.4	2.7	15	23.2–27.0
10	16	RSL	IV	2.1	3.1	15	31.0–35.9
10	17	LSL	IV	0.5	0.5	5.4	6.7–7.4
11	18	ILL	IV	7.8	0.8	6.1	23.3–24.2
12	19	LSL	IV	0.1	1.7	15	22.4–25.1
13	20	IRL	IIIb	11.4	27	137	85.0–121.5
14	21	RSL	Ia	2.2	1.7	10	23.4–23.4
15	22	RSL	IV	0.2	0.9	3.2	13.9–15.8
16	23	RSL	IV	2.2	3.9	22	25.8–29.4
17	24	LSL	IV	3.1	9.8	28	49.3–52.9
18	25	RSL	IV	8.1	0.6	3.3	7.7–8.5
19	26	LSL	IV	1.4	0.8	5.9	12.0–12.4

cc, cubic centimeters; RSL, right superior lung; IRL, inferior right lung; LSL, left superior lung; ILL, inferior left lung; RCS right cardiophrenic space; CTV, clinical target volume; PTV_{SBRT}, SBRT planning target volume; PTV_{PT}, field-specific target volume;

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